Search in UniProt Knowledgebase (Swiss-Prot and TrEMBL) for: non-receptor protein kinase

UniProtKB/Swiss-Prot Release 47.6 of 02-Aug-2005
UniProtKB/TrEMBL Release 30.6 of 02-Aug-2005

- Number of sequences found in UniProt Knowledgebase (Swiss-Prot$_{(8)}$ and TrEMBL)$_{(8)}$: **16**
- Note that the selected sequences can be saved to a file to be later retrieved; to do so, go to the bottom of this page.
- For more directed searches, you can use the Sequence Retrieval System SRS.

Search in UniProtKB/Swiss-Prot: There are matches to 8 out of 188752 entries

ACK1_HUMAN (**Q07912**)
Activated CDC42 kinase 1 (EC 2.7.1.112) (ACK-1) (Tyrosine kinase non-receptor protein 2). {GENE: Name=TNK2; Synonyms=ACK1} - Homo sapiens (Human)

ACK1_MOUSE (**O54967**)
Activated CDC42 kinase 1 (EC 2.7.1.112) (ACK-1) (Non-receptor protein tyrosine kinase Ack) (Tyrosine kinase non-receptor protein 2). {GENE: Name=Tnk2; Synonyms=Ack1} - Mus musculus (Mouse)

DUS1_RAT (**Q64623**)
Dual specificity protein phosphatase 1 (EC 3.1.3.48) (EC 3.1.3.16) (MAP kinase phosphatase-1) (MKP-1) (Protein-tyrosine phosphatase CL100) (Protein-tyrosine phosphatase non-receptor type 16). {GENE: Name=Dusp1; Synonyms=Cl100, Ptpn16} - Rattus norvegicus (Rat)

KYK1_DICDI (**P18160**)
Non-receptor tyrosine kinase spore lysis A (EC 2.7.1.112) (Tyrosine-protein kinase 1). {GENE: Name=splA; Synonyms=dpyK1, pykA} - Dictyostelium discoideum (Slime mold)

TNK1_HUMAN (**Q13470**)
Non-receptor tyrosine-protein kinase TNK1 (EC 2.7.1.112) (CD38 negative kinase 1). {GENE: Name=TNK1} - Homo sapiens (Human)

TNK1_MOUSE (**Q99ML2**)
Non-receptor tyrosine-protein kinase TNK1 (EC 2.7.1.112) (Kinase of embryonic stem cells). {GENE: Name=Tnk1; Synonyms=Kos1} - Mus musculus (Mouse)

TYK2_HUMAN (**P29597**)
Non-receptor tyrosine-protein kinase TYK2 (EC 2.7.1.112). {GENE: Name=TYK2} - Homo sapiens (Human)

TYK2_MOUSE (**Q9R117**)
Non-receptor tyrosine-protein kinase TYK2 (EC 2.7.1.112). {GENE: Name=Tyk2} - Mus

musculus (Mouse)

Search in UniProtKB/TrEMBL: There are matches to 8 out of 1942311 entries

O45232_CAEEL
Hypothetical protein ark-1 (Ack related non-receptor tyrosine kinase) {GENE:Name=ark-1; ORFNames=C01C7.1} - Caenorhabditis elegans

O61731_HYDAT
Non-receptor protein-tyrosine kinase Abl (Fragment) - Hydra attenuata (Hydra) (Hydra vulgaris)

O77132_HYDAT
Non-receptor protein-tyrosine kinase CSK {GENE:Name=CSK} - Hydra attenuata (Hydra) (Hydra vulgaris)

O93411_XENLA
Non-receptor protein tyrosine kinase laloo - Xenopus laevis (African clawed frog)

Q75K08_DICDI
Non-receptor tyrosine kinase spore lysis A (EC 2.7.1.112) (Tyrosine-protein kinase 1) (Hypothetical protein) {GENE:ORFNames=DDB0169187} - Dictyostelium discoideum (Slime mold)

Q86IU5_DICDI
Similar to Dictyostelium discoideum (Slime mold). Non-receptor tyrosine kinase spore lysis A (EC 2.7.1.112) (Tyrosine-protein kinase 1) - Dictyostelium discoideum (Slime mold)

Q86J21_DICDI
Non-receptor tyrosine kinase spore lysis A (EC 2.7.1.112) (Tyrosine-protein kinase 1) (Hypothetical protein) {GENE:ORFNames=DDB0167822} - Dictyostelium discoideum (Slime mold)

Q86K52_DICDI
Non-receptor tyrosine kinase spore lysis A (EC 2.7.1.112) (Tyrosine-protein kinase 1) (Hypothetical protein) {GENE:ORFNames=DDB0169123} - Dictyostelium discoideum (Slime mold)

New Search
in Swiss-Prot/TrEMBL by AC, ID, description, gene name, organism
Please do NOT use any boolean operators (and, or, etc.)

If you would like to retrieve all the Swiss-Prot/TrEMBL entries contained in this list , you can enter a file name. These entries will then be saved to a file under this name in the directory `outgoing` of the ExPASy anonymous ftp server, from where you can download it. (Please note that this temporary file will only be kept for 1 week.)

File name:

Format: ◉ Swiss-Prot ○ Fasta

Reset or Create file

Search in UniProt Knowledgebase (Swiss-Prot and TrEMBL) for: pyk2

UniProtKB/Swiss-Prot Release 47.6 of 02-Aug-2005
UniProtKB/TrEMBL Release 30.6 of 02-Aug-2005

- Number of sequences found in UniProt Knowledgebase (Swiss-Prot)(14) and TrEMBL)(10): **24**
- Note that the selected sequences can be saved to a file to be later retrieved; to do so, go to the bottom of this page.
- For more directed searches, you can use the Sequence Retrieval System SRS.

Search in UniProtKB/Swiss-Prot: There are matches to 14 out of 188752 entries

DDEF2_HUMAN (**O43150**)
Development and differentiation-enhancing factor 2 (Pyk2 C-terminus associated protein) (PAP) (Paxillin-associated protein with ARFGAP activity 3) (PAG3). {GENE: Name=DDEF2; Synonyms=KIAA0400} - Homo sapiens (Human)

DDEF2_MOUSE (**Q7SIG6**)
Development and differentiation-enhancing factor 2 (Pyk2 C-terminus associated protein) (PAP) (Paxillin-associated protein with ARFGAP activity 3) (PAG3). {GENE: Name=Ddef2} - Mus musculus (Mouse)

ELF3_ARATH (**O82804**)
EARLY FLOWERING 3 protein (Nematode responsive protein). {GENE: Name=ELF3; Synonyms=PYK20; OrderedLocusNames=At2g25930; ORFNames=F17H15.25, T19L18.26} - Arabidopsis thaliana (Mouse-ear cress)

FAK2_HUMAN (**Q14289**)
Protein tyrosine kinase 2 beta (EC 2.7.1.112) (Focal adhesion kinase 2) (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase beta) (CAK beta) (Calcium-dependent tyrosine kinase) (CADTK) (Related adhesion focal tyrosine kinase). {GENE: Name=PTK2B; Synonyms=FAK2, PYK2, RAFTK} - Homo sapiens (Human)

FAK2_MOUSE (**Q9QVP9**)
Protein tyrosine kinase 2 beta (EC 2.7.1.112) (Focal adhesion kinase 2) (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase beta) (CAK beta) (Calcium-dependent tyrosine kinase) (CADTK) (Related adhesion focal tyrosine kinase). {GENE: Name=Ptk2b; Synonyms=Fak2, Pyk2, Raftk} - Mus musculus (Mouse)

FAK2_RAT (**P70600**)
Protein tyrosine kinase 2 beta (EC 2.7.1.112) (Focal adhesion kinase 2) (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase beta) (CAK beta) (Calcium-dependent tyrosine kinase)

(CADTK). {GENE: Name=Ptk2b; Synonyms=Fak2, Pyk2} - Rattus norvegicus (Rat)

KPYK2_AGRVI (**Q44473**)
Pyruvate kinase (EC 2.7.1.40) (PK). {GENE: Name=ttuE} - Agrobacterium vitis (Rhizobium vitis)

KPYK2_CANGA (**Q6FV12**)
Pyruvate kinase 2 (EC 2.7.1.40) (PK 2). {GENE: Name=PYK2; OrderedLocusNames=CAGL0E05610g} - Candida glabrata (Yeast) (Torulopsis glabrata)

KPYK2_ECOLI (**P21599**)
Pyruvate kinase II (EC 2.7.1.40) (PK-2). {GENE: Name=pykA; OrderedLocusNames=b1854} - Escherichia coli

KPYK2_SALTY (**Q8ZNW0**)
Pyruvate kinase II (EC 2.7.1.40) (PK-2). {GENE: Name=pykA; OrderedLocusNames=STM1888} - Salmonella typhimurium

KPYK2_SYNY3 (**P73534**)
Pyruvate kinase 2 (EC 2.7.1.40) (PK 2). {GENE: Name=pyk2; OrderedLocusNames=sll1275} - Synechocystis sp. (strain PCC 6803)

KPYK2_TRYBB (**P30616**)
Pyruvate kinase 2 (EC 2.7.1.40) (PK 2). {GENE: Name=PYK2} - Trypanosoma brucei brucei

KPYK2_YEAST (**P52489**)
Pyruvate kinase 2 (EC 2.7.1.40) (PK 2). {GENE: Name=PYK2; OrderedLocusNames=YOR347C; ORFNames=O6342} - Saccharomyces cerevisiae (Baker's yeast)

KYK2_DICDI (**P18161**)
Tyrosine-protein kinase 2 (EC 2.7.1.112) (Fragment). {GENE: Name=splB; Synonyms=dpyK2, pykB} - Dictyostelium discoideum (Slime mold)

Search in UniProtKB/TrEMBL: There are matches to 10 out of 1942311 entries

Q4PYK2_9HIV1
Reverse transcriptase (Fragment) {GENE:Name=pol} - Human immunodeficiency virus 1

Q5PYK2_9FILI
Ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit (Fragment) {GENE:Name=rbcL} - Elaphoglossum lindenii [Chloroplast]

Q65G83_BACLD
Pyruvate kinase (EC 2.7.1.40) {GENE:Name=pyk2; OrderedLocusNames=BLi03067} - Bacillus licheniformis (strain DSM 13 / ATCC 14580)

Q7PYK2_ANOGA
ENSANGP00000018482 (Fragment) {GENE:ORFNames=ENSANGG00000015993} - Anopheles gambiae str. PEST

Q7T2P8_BRARE
Proline-rich tyrosine kinase 2 (EC 2.7.1.112) (Protein tyrosine kinase 2 beta) {GENE:Name=ptk2b; Synonyms=pyk2; ORFNames=CH211-142K18.3-001} - Brachydanio rerio (Zebrafish) (Danio rerio)

Q866G6_DIDMA
Non-receptor tyrosine kinase Pyk2 (Fragment) - Didelphis marsupialis virginiana (North American opossum)

Q876K4_SACBA
PYK2 - Saccharomyces bayanus (Yeast) (Saccharomyces uvarum)

Q8EX62_LEPIN

Pyruvate kinase (EC 2.7.1.40) {GENE:Name=pyk2; OrderedLocusNames=LB353} - Leptospira interrogans

Q8PYK2_METMA
Conserved protein {GENE:OrderedLocusNames=MM0859} - Methanosarcina mazei (Methanosarcina frisia)

Q9PYK2_HTLV2
Envelope glycoprotein (Fragment) {GENE:Name=env} - Human T-cell leukemia virus type II. (HTLV-II)

New Search
in Swiss-Prot/TrEMBL by AC, ID, description, gene name, organism
Please do NOT use any boolean operators (and, or, etc.)

If you would like to retrieve all the Swiss-Prot/TrEMBL entries contained in this list , you can enter a file name. These entries will then be saved to a file under this name in the directory `outgoing` of the ExPASy anonymous ftp server, from where you can download it. (Please note that this temporary file will only be kept for 1 week.)

File name:

Format: Swiss-Prot Fasta

Reset or Create file

UniProtKB/Swiss-Prot entry Q07912

Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.

Entry information

Entry name	**ACK1_HUMAN**
Primary accession number	**Q07912**
Secondary accession numbers	Q8N6U7 Q96H59
Entered in Swiss-Prot in	Release 43, March 2004
Sequence was last modified in	Release 43, March 2004
Annotations were last modified in	Release 48, September 2005

Name and origin of the protein

Protein name	**Activated CDC42 kinase 1**
Synonyms	**EC 2.7.1.112** **ACK-1** **Tyrosine kinase non-receptor protein 2**
Gene name	**Name: TNK2** Synonyms: ACK1
From	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini; Hominidae; Homo.

References

[1] NUCLEOTIDE SEQUENCE (ISOFORM 1), AND INTERACTION WITH CDC42.
TISSUE=Hippocampus;
DOI=10.1038/363364a0; PubMed=8497321 [NCBI, ExPASy, EBI, Israel, Japan]
Manser E., Leung T., Salihuddin H., Tan L., Lim L.;
"A non-receptor tyrosine kinase that inhibits the GTPase activity of p21cdc42.";
Nature 363:364-367(1993).

[2] NUCLEOTIDE SEQUENCE [LARGE SCALE MRNA] (ISOFORM 2).
TISSUE=Brain, and Uterus;
DOI=10.1073/pnas.242603899; PubMed=12477932 [NCBI, ExPASy, EBI, Israel, Japan]
Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G., Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D., Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K., Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., [redacted], Marra M.A.;
"Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences.";
Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).

[3] PHOSPHORYLATION SITES TYR-826; TYR-857 AND TYR-858.
DOI=10.1073/pnas.2436191100; PubMed=12522270 [NCBI, ExPASy, EBI, Israel, Japan]
Salomon A.R., Ficarro S.B., Brill L.M., Brinker A., Phung Q.T., Ericson C., Sauer K., Brock A., Horn D.M., Schultz P.G., Peters E.C.;
"Profiling of tyrosine phosphorylation pathways in human cells using mass spectrometry.";
Proc. Natl. Acad. Sci. U.S.A. 100:443-448(2003).

[4] STRUCTURE BY NMR OF 448-489.
DOI=10.1038/20732; PubMed=10360579 [NCBI, ExPASy, EBI, Israel, Japan]
Mott H.R., Owen D., Nietlispach D., Lowe P.N., Manser E., Lim L., Laue E.D.;
"Structure of the small G protein Cdc42 bound to the GTPase-binding domain of ACK.";
Nature 399:384-388(1999).

Comments

- ***FUNCTION***: Tyrosine kinase, that after binding to CDC42, inhibits both its intrinsic and stimulated GTPase activity.
- ***CATALYTIC ACTIVITY***: ATP + a protein tyrosine = ADP + a protein tyrosine phosphate.
- ***SUBUNIT***: Interacts with CDC42.
- ***ALTERNATIVE PRODUCTS***:
  Display all isoform sequences in FASTA format
  - **Alternative splicing [2 named forms]**

    Name 1
    Isoform ID Q07912-1
    This is the isoform sequence displayed in this entry.

    Name 2
    Isoform ID Q07912-2
    Note: No experimental confirmation available.
    Features which should be applied to build the isoform sequence: VSP_008655, VSP_008656.

- ***SIMILARITY***: Belongs to the Tyr protein kinase family.
- ***SIMILARITY***: Contains 1 CRIB domain.
- ***SIMILARITY***: Contains 1 SH3 domain.

Copyright

Cross-references

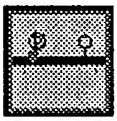
EMBL	L13738; AAA53570.2; -; mRNA. [EMBL / GenBank / DDBJ] [CoDingSequence] BC008884; AAH08884.1; -; mRNA. [EMBL / GenBank / DDBJ] [CoDingSequence] BC028164; AAH28164.1; -; mRNA. [EMBL / GenBank / DDBJ] [CoDingSequence]
PIR	S33596; S33596.
PDB	1CF4; NMR; B=448-489. [ExPASy / RCSB / EBI] 1U46; X-ray; A/B=109-395. [ExPASy / RCSB / EBI] 1U4D; X-ray; A/B=109-395. [ExPASy / RCSB / EBI] 1U54; X-ray; A/B=109-395. [ExPASy / RCSB / EBI] Detailed list of linked structures.
Ensembl	ENSG00000061938; Homo sapiens: [Contig view]
HGNC	HGNC:19297; TNK2.

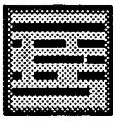
CleanEx	HGNC:19297; TNK2.
GeneCards	TNK2.
GeneLynx	TNK2; Homo sapiens.
GenAtlas	TNK2.
MIM	606994 [NCBI / EBI].
SOURCE	TNK2; Homo sapiens.
GO	GO:0005095; Molecular function: GTPase inhibitor activity *(traceable author statement)*. GO:0004715; Molecular function: non-membrane spanning protein tyrosine kinase activity *(traceable author statement)*. GO:0007264; Biological process: small GTPase mediated signal transduction *(traceable author statement)*. QuickGo view.
InterPro	IPR000095; PAKbox/Rhobndng. IPR000719; Prot_kinase. IPR001452; SH3. IPR001245; Tyr_pkinase. IPR008266; Tyr_pkinase_AS. IPR000449; UBA. Graphical view of domain structure.
Pfam	PF00018; SH3_1; 1. PF00627; UBA; 1. Pfam graphical view of domain structure.
PRINTS	PR00109; TYRKINASE.
ProDom	PD000001; Prot_kinase; 1. [Domain structure / List of seq. sharing at least 1 domain]
PROSITE	PS50108; CRIB; FALSE_NEG. PS00107; PROTEIN_KINASE_ATP; 1. PS50011; PROTEIN_KINASE_DOM; 1. PS00109; PROTEIN_KINASE_TYR; 1. PS50002; SH3; 1. PROSITE graphical view of domain structure (profiles).
HOVERGEN	[Family / Alignment / Tree]
BLOCKS	Q07912.
ProtoNet	Q07912.
ProtoMap	Q07912.
PRESAGE	Q07912.
DIP	Q07912.
ModBase	Q07912.
SWISS-2DPAGE	Get region on 2D PAGE.
UniRef	View cluster of proteins with at least 50% / 90% identity.

Keywords

3D-structure; **Alternative splicing**; **ATP-binding**; **Kinase**; **Nucleotide-binding**; **Phosphorylation**; **SH3 domain**; **Transferase**; **Tyrosine-protein kinase**.

Features

 Feature table viewer

 Feature aligner

Key	From	To	Length	Description	FTId
DOMAIN	126	385	260	Protein kinase.	
DOMAIN	386	448	63	SH3.	
DOMAIN	454	466	13	CRIB.	
NP_BIND	132	140	9	ATP *(By similarity)*.	
COMPBIAS	577	956	380	Pro-rich.	
ACT_SITE	252	252		Proton acceptor *(By similarity)*.	
BINDING	158	158		ATP *(By similarity)*.	
MOD_RES	826	826		Phosphotyrosine.	
MOD_RES	857	857		Phosphotyrosine.	
MOD_RES	858	858		Phosphotyrosine.	
VARSPLIC	485	528		LYLGNPMDPPDLLSVELSTSRPPQHLGGVKKPTYDPVSE DQDPL -> CPFSAFSPGHPPAETCGQVLWTGRREACASDPRLHPVSS RTKGL (in isoform 2).	VSP_008655
VARSPLIC	529	1036		Missing (in isoform 2).	VSP_008656
CONFLICT	138	138		G -> V (in Ref. 2; AAH08884).	
CONFLICT	304	352		TRTFSHASDTWMFGVTLWEMFTYGQEPWIGLNGSQILHKI DKEGERLPR -> PPWRDISASSSTQFPHAVPCFPTSLLAKLLLRHSVPASSR EIKLVSILC (in Ref. 2; AAH08884).	
CONFLICT	353	1036		Missing (in Ref. 2; AAH08884).	

Sequence information

Length: **1036** **AA** Molecular weight: **114327 Da** CRC64: **B9B90BA7E3E22DFF** [This is a checksum on the sequence]

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        70         80         90        100        110        120
EAVKRRKALC KRKSWMSKVF SGKRLEAEFP PHHSQSTFRK TSPAPGGPAG EGPLQSLTCL

       130        140        150        160        170        180
IGEKDLRLLE KLGDGSFGVV RRGEWDAPSG KTVSVAVKCL KPDVLSQPEA MDDFIREVNA

       190        200        210        220        230        240
MHSLDHRNLI RLYGVVLTPP MKMVTELAPL GSLLDRLRKH QGHFLLGTLS RYAVQVAEGM

       250        260        270        280        290        300
GYLESKRFIH RDLAARNLLL ATRDLVKIGD FGLMRALPQN DDHYVMQEHR KVPFAWCAPE

       310        320        330        340        350        360
SLKTRTFSHA SDTWMFGVTL WEMFTYGQEP WIGLNGSQIL HKIDKEGERL PRPEDCPQDI

       370        380        390        400        410        420
YNVMVQCWAH KPEDRPTFVA LRDFLLEAQP TDMRALQDFE EPDKLHIQMN DVITVIEGRA

       430        440        450        460        470        480
ENYWWRGQNT RTLCVGPFPR NVVTSVAGLS AQDISQPLQN SFIHTGHGDS DPRHCWGFPD
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       490        500        510        520        530        540
RIDELYLGNP MDPPDLLSVE LSTSRPPQHL GGVKKPTYDP VSEDQDPLSS DFKRLGLRKP

       550        560        570        580        590        600
GLPRGLWLAK PSARVPGTKA SRGSGAEVTL IDFGEEPVVP ALRPCPPSLA QLAMDACSLL

       610        620        630        640        650        660
DETPPQSPTR ALPRPLHPTP VVDWDARPLP PPPAYDDVAQ DEDDFEICSI NSTLVGAGVP

       670        680        690        700        710        720
AGPSQGQTNY AFVPEQARPP PPLEDNLFLP PQGGGKPPSS AQTAEIFQAL QQECMRQLQA

       730        740        750        760        770        780
PGSPAPSPSP GGDDKPQVPP RVPIPPRPTR PHVQLSPAPP GEEETSQWPG PASPPRVPPR

       790        800        810        820        830        840
EPLSPQGSRT PSPLVPPGSS PLPPRLSSSP GKTMPTTQSF ASDPKYATPQ VIQAPGAGGP

       850        860        870        880        890        900
CILPIVRDGK KVSSTHYYLL PERPSYLERY QRFLREAQSP EEPTPLPVPL LLPPPSTPAP

       910        920        930        940        950        960
AAPTATVRPM PQAALDPKAN FSTNNSNPGA RPPPPRATAR LPQRGCPGDG PEAGRPADKI

       970        980        990       1000       1010       1020
QMAMVHGVTT EECQAALQCH GWSVQRAAQY LKVEQLFGLG LRPRGECHKV LEMFDWNLEQ

      1030
AGCHLLGSWG PAHHKR
```

Q07912 in FASTA format

View entry in original UniProtKB/Swiss-Prot format
View entry in raw text format (no links)
Report form for errors/updates in this UniProtKB/Swiss-Prot entry

BLAST submission on ExPASy/SIB or at NCBI (USA)

Sequence analysis tools: ProtParam, ProtScale, Compute pI/Mw, PeptideMass, PeptideCutter, Dotlet (Java)

ScanProsite, MotifScan

Submit a homology modeling request to SWISS-MODEL

NPSA Sequence analysis tools

==========

Welcome to the SIB BLAST Network Service

If results of this search are reported or published, please mention that the computation was performed at the SIB using the BLAST network service. The SIB BLAST network service uses a server developed at SIB and the NCBI BLAST 2 software.

In case of problems, please read the online BLAST help.
If your question is not covered, please contact <helpdesk@expasy.org>.

NCBI BLAST program reference [PMID:9254694]:
Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

==========

Query: 1009 AA (of which 5% low-complexity regions filtered out)
Date run: 2005-08-10 10:15:40 UTC+0100 on sib-gm1.unil.ch
Program: NCBI BLASTP 1.5.4-Paracel [2003-06-05]
Database: EXPASY/UniProtKB
2,142,762 sequences; 699,641,365 total letters
UniProt Knowledgebase Release 5.6 consists of:
UniProtKB/Swiss-Prot Release 47.6 of 02-Aug-2005: 188752 entries
UniProtKB/TrEMBL Release 30.6 of 02-Aug-2005: 1942311 entries

Taxonomic view | NiceBlast view | Printable view

List of potentially matching sequences

Send selected sequences to Clustal W (multiple alignment) Submit Query
Select up to...

☐ Include query sequence

	Db	AC	Description	Score	E-va
☐	sp	Q14289	FAK2_HUMAN Protein tyrosine kinase 2 beta (EC 2.7.1.11...	1914	
☐	tr	Q6PID4	_HUMAN PTK2B protein tyrosine kinase 2 beta, isoform a ...	1912	
☐	tr	Q5R7F6	_PONPY Hypothetical protein DKFZp459L1823 [DKFZp459L182...	1894	
☐	sp	P70600	FAK2_RAT Protein tyrosine kinase 2 beta (EC 2.7.1.112)...	1844	
☐	sp	Q9QVP9	FAK2_MOUSE Protein tyrosine kinase 2 beta (EC 2.7.1.11...	1838	
☐	sp_vs	Q14289-2	Splice isoform 2 of Q14289 [PTK2B] [Homo sapiens ...	1804	
☐	sp_vs	P70600-3	Splice isoform 3 of P70600 [Ptk2b] [Rattus norveg...	1734	
☐	tr	Q8C2G0	_MOUSE Mus musculus 2 days neonate thymus thymic cells ...	1727	
☐	tr	Q59GM4	_HUMAN PTK2B protein tyrosine kinase 2 beta isoform a v...	1506	

tr	Q5XH98	_XENTR Hypothetical LOC496459 [LOC496459] [Xenopus trop...	1234	
tr	Q7T2P8	_BRARE Proline-rich tyrosine kinase 2 (EC 2.7.1.112) (P...	1109	
tr	Q6ZRA8	_HUMAN Hypothetical protein FLJ46514 [Homo sapiens (Hum...	1003	
tr	Q4RR57	_TETNG Chromosome 14 SCAF15003, whole genome shotgun se...	998	
tr	Q4RY69	_TETNG Chromosome 3 SCAF14978, whole genome shotgun seq...	937	
tr	Q8C6R5	_MOUSE Mus musculus 2 days pregnant adult female oviduc...	815	
tr	Q8C9L4	_MOUSE Mus musculus 3 days neonate thymus cDNA, RIKEN f...	811	
tr	Q8IYN9	_HUMAN PTK2 protein [PTK2] [Homo sapiens (Human)]	769	
tr	Q98SN4	_BRARE Focal adhesion kinase 1a [ptk2.1] [Brachydanio r...	769	
sp_vs	Q91738-2	Splice isoform Short of Q91738 [FAK1] [Xenopus la...	769	
tr	Q7T2V4	_BRARE Focal adhesion kinase 1b [ptk2.2] [Brachydanio r...	768	
tr	Q5DTH7	_MOUSE MKIAA4203 protein (Fragment) [Ptk2] [Mus musculu...	766	
sp	O35346	FAK1_RAT Focal adhesion kinase 1 (EC 2.7.1.112) (FADK ...	766	
sp	Q05397	FAK1_HUMAN Focal adhesion kinase 1 (EC 2.7.1.112) (FAD...	766	
tr	Q658W2	_HUMAN Hypothetical protein DKFZp666O0110 [DKFZp666O011...	766	
sp	Q00944	FAK1_CHICK Focal adhesion kinase 1 (EC 2.7.1.112) (FAD...	765	
sp_vs	P34152-3	Splice isoform 3 of P34152 [Ptk2] [Mus musculus (...	764	
tr	Q8C513	_MOUSE Mus musculus 0 day neonate thymus cDNA, RIKEN fu...	763	
sp	Q91738	FAK1_XENLA Focal adhesion kinase 1 (EC 2.7.1.112) (FAD...	759	
tr	Q6IR54	_XENLA MGC83487 protein [MGC83487] [Xenopus laevis (Afr...	759	
sp_vs	P34152-2	Splice isoform 2 of P34152 [Ptk2] [Mus musculus (...	753	
sp	P34152	FAK1_MOUSE Focal adhesion kinase 1 (EC 2.7.1.112) (FAD...	747	
tr	Q4SH73	_TETNG Chromosome 8 SCAF14587, whole genome shotgun seq...	699	
tr	Q59GN8	_HUMAN PTK2 protein tyrosine kinase 2 isoform b variant...	695	
tr	Q59GM6	_HUMAN PTK2 protein tyrosine kinase 2 isoform b variant...	694	
tr	Q7Z1D3	_LYTVA Focal adhesion kinase [Lytechinus variegatus (Se...	670	
tr	Q8K2S0	_MOUSE Ptk2 protein [Ptk2] [Mus musculus (Mouse)]	640	
tr	Q8CHM2	_MOUSE Focal adhesion kinase spliced variant p110FAK [P...	621	e-
sp_vs	Q05397-2	Splice isoform 2 of Q05397 [PTK2] [Homo sapiens (...	615	e-
tr	Q7QHB8	_ANOGA ENSANGP00000008377 (Fragment) [ENSANGG0000000632...	518	e-
tr	Q5MCM8	_HYDEC Protein-tyrosine kinase (Fragment) [FAK] [Hydrac...	507	e-
tr	Q8N9D7	_HUMAN Hypothetical protein FLJ37680 [Homo sapiens (Hum...	499	e-
tr	Q5MB01	_HYDMA Protein-tyrosine kinase (Fragment) [FAK] [Hydra ...	468	e-
sp_vs	Q05397-3	Splice isoform 3 of Q05397 [PTK2] [Homo sapiens (...	468	e-
tr	Q9U531	_DROME Focal adhesion kinase homolog DFak56 [Fak56D] [D...	466	e-
tr	Q9U472	_DROME Focal adhesion kinase homolog FAK56 [Fak56D] [Dr...	465	e-
tr	Q9V8U8	_DROME CG10023-PA, isoform A (Cg10023-pb, isoform b) [F...	465	e-
tr	Q5BIG9	_DROME RE57482p [Fak56D] [Drosophila melanogaster (Frui...	457	e-
tr	Q9U5Y2	_DROME Focal adhesion kinase (EC 2:7.1.112) [Fak56D] [D...	454	e-
sp_vs	P70600-2	Splice isoform 2 of P70600 [Ptk2b] [Rattus norveg...	398	e-
tr	Q8CFH7	_MOUSE Focal adhesion kinase [Ptk2] [Mus musculus (Mouse)]	334	8e
sp_vs	Q05397-4	Splice isoform 4 of Q05397 [PTK2] [Homo sapiens (...	322	3e
tr	Q4SJ17	_TETNG Chromosome 21 SCAF14577, whole genome shotgun se...	310	2e
tr	Q61HB9	_CAEBR Hypothetical protein CBG10801 [CBG10801] [Caenor...	307	8e
tr	Q4SJ18	_TETNG Chromosome 21 SCAF14577, whole genome shotgun se...	305	4e

☐	tr	Q95YD4	_CAEEL Protein kinase protein 32, isoform a [kin-32] [C...	301	4e
☐	tr	Q8T879	_CAEEL Protein kinase protein 32, isoform b [kin-32] [C...	295	5e
☐	tr	Q866G6	_DIDMA Non-receptor tyrosine kinase Pyk2 (Fragment) [Di...	278	7e
☐	tr	Q7SXQ6	_BRARE Ptk2.1 protein [ptk2.1] [Brachydanio rerio (Zebr...	274	1e
☐	tr	Q4S351	_TETNG Chromosome 4 SCAF14752, whole genome shotgun seq...	218	8e
☐	tr	Q6PEE5	_MOUSE Fert2 protein [Fert2] [Mus musculus (Mouse)]	214	7e
☐	tr	P70451	_MOUSE Fer [Fert2] [Mus musculus (Mouse)]	214	7e
☐	tr	Q80UI3	_MOUSE Fert2 protein (Fragment) [Fert2] [Mus musculus (...	214	7e
☐	tr	Q8C481	_MOUSE Mus musculus ES cells cDNA, RIKEN full-length en...	214	7e
☐	sp	P09760	FLK_RAT Tyrosine-protein kinase FLK (EC 2.7.1.112) (Fr...	213	2e
☐	tr	Q9TTY2	_CANFA Protein tyrosine kinase fer [Canis familiaris (D...	213	2e
☐	tr	Q61561	_MOUSE Tyrosine kinase (ferT) [Fert2] [Mus musculus (Mo...	211	6e
☐	sp	P16591	FER_HUMAN Proto-oncogene tyrosine-protein kinase FER (...	211	8e
☐	tr	O77440	_HYDAT Protein-tyrosine kinase HTK98 [HTK98] [Hydra att...	200	1e
☐	tr	Q9Y1Y3	_9METZ Protein tyrosine kinase [EfPTK56] [Ephydatia flu...	199	2e
☐	sp	Q15303	ERBB4_HUMAN Receptor tyrosine-protein kinase erbB-4 pr...	199	4e
☐	tr	Q59EW4	_HUMAN V-erb-a erythroblastic leukemia viral oncogene h...	199	4e
☐	sp_vs	Q15303-2	Splice isoform JM-B of Q15303 [ERBB4] [Homo sapie...	199	4e
☐	sp	Q62956	ERBB4_RAT Receptor tyrosine-protein kinase erbB-4 prec...	198	5e
☐	tr	Q9W6F6	_CHICK Receptor tyrosine kinase (Fragment) [erbB4] [Gal...	198	5e
☐	tr	Q6UA29	_RAT Receptor tyrosine kinase isoform JMa cyt1 [Erbb4] ...	198	5e
☐	tr	Q6UA28	_RAT Receptor tyrosine kinase isoform JMa cyt2 [Erbb4] ...	198	5e
☐	tr	Q4PLA5	_CHICK Ovarian receptor tyrosine kinase erbB4 precusor ...	197	1e
☐	tr	Q4PLA4	_CHICK Ovarian receptor tyrosine kinase erbB4 precusor ...	197	1e
☐	sp	P09759	EPHB1_RAT Ephrin type-B receptor 1 precursor (EC 2.7.1...	197	2e
☐	sp	Q91736	EPB1B_XENLA Ephrin type-B receptor 1B (EC 2.7.1.112) (...	197	2e
☐	sp	Q91694	EPA4B_XENLA Ephrin type-A receptor 4B precursor (EC 2....	197	2e
☐	tr	Q7SZF7	_BRARE Epidermal growth factor receptor [egfr] [Brachyd...	197	2e
☐	tr	Q6VQA3	_BRARE Epidermal growth factor receptor [egfr] [Brachyd...	197	2e
☐	tr	Q8CBF3	_MOUSE Mus musculus 16 days neonate cerebellum cDNA, RI...	197	2e
☐	tr	Q8CBE2	_MOUSE Mus musculus 16 days neonate cerebellum cDNA, RI...	197	2e
☐	sp	P54762	EPHB1_HUMAN Ephrin type-B receptor 1 precursor (EC 2.7...	196	2e
☐	tr	Q7ZYM7	_XENLA Pag protein [pag] [Xenopus laevis (African clawe...	196	2e
☐	tr	Q9Y1Y2	_9METZ Protein tyrosine kinase [EfPTK62] [Ephydatia flu...	196	2e
☐	sp_vs	P54762-2	Splice isoform 2 of P54762 [EPHB1] [Homo sapiens ...	196	2e
☐	tr	Q7QAK4	_ANOGA ENSANGP00000020257 (Fragment) [ENSANGG0000001776...	196	3e
☐	tr	Q4SQX3	_TETNG Chromosome 11 SCAF14528, whole genome shotgun se...	195	4e
☐	tr	Q6GNQ8	_XENLA MGC80946 protein [MGC80946] [Xenopus laevis (Afr...	195	6e
☐	tr	Q9Y1Y1	_9METZ Protein tyrosine kinase (Fragment) [EfPTK79] [Ep...	195	6e
☐	sp	P54755	EPHA5_CHICK Ephrin type-A receptor 5 precursor (EC 2.7...	194	1e
☐	sp	Q91845	EPA4A_XENLA Ephrin type-A receptor 4A precursor (EC 2....	194	1e
☐	sp_vs	P54755-2	Splice isoform 1 of P54755 [EPHA5] [Gallus gallus...	194	1e
☐	sp_vs	P54755-3	Splice isoform 2 of P54755 [EPHA5] [Gallus gallus...	194	1e
☐	sp	Q07497	EPHB5_CHICK Ephrin type-B receptor 5 precursor (EC 2.7...	194	1e
☐	sp	Q07494	EPHB1_CHICK Ephrin type-B receptor 1 (EC 2.7.1.112) (T...	194	1e

☐ sp P00521 ABL_MLVAB Tyrosine-protein kinase transforming protein... 194 1e

Graphical overview of the alignments

Click here to resubmit your query after masking regions matching PROSITE profiles or Pfam HMMs

(? Help) (use ScanProsite for more details about PROSITE matches)


Matches on query sequence
Mat
Submission
1
500
1000
1
FAK2_HUMAN
Q6PID4
Q5R7F6
FAK2_RAT
FAK2_MOUSE
FAK2_HUMAN-2
FAK2_RAT-3
Q8C2G0
Q59GM4
Q5XH98
Q7T2P8
Q6ZRA8
Q4RR57
Q4RY69
Q8C6R5
Q8C9L4
Q8IYN9
Q98SN4
FAK1_XENLA-2
Q7T2V4
Q5DTH7
FAK1_RAT
FAK1_HUMAN
Q658W2
FAK1_CHICK
FAK1_MOUSE-3
Q8C513
FAK1_XENLA
Q6IR54
FAK1_MOUSE-2
FAK1_MOUSE
Q4SH73
Q59GN8
Q59GM6
Q7Z1D3
Q8K2S0
Q8CHM2
FAK1_HUMAN-2
Q7QHB8
Q5MCM8
Q8N9D7
Q5MB01
FAK1_HUMAN-3
Q9U531
Q9U472
Q9V8U8
Q5BIG9
Q9U5Y2
FAK2_RAT-2
Q8CFH7
FAK1_HUMAN-4
Q4SJ17
Q61HB9
Q4SJ18
Q95YD4
Q8T879
Q866G6
Q7SXQ6
Q4S351
Q6PEE5
P70451
Q80UI3
Q8C481
FLK_RAT
Q9TTY2
Q61561
FER_HUMAN
O77440
Q9Y1Y3
ERBB4_HUMAN
Q59EW4
ERBB4_HUMAN-2
ERBB4_RAT
Q9W6F6
Q6UA29
Q6UA28
Q4PLA5
Q4PLA4
EPHB1_RAT
EPB1B_XENLA
EPA4B_XENLA
Q7SZF7
Q6VQA3
Q8CBF3
Q8CBE2
EPHB1_HUMAN

Alignments

sp Q14289 FAK2_HUMAN **Protein tyrosine kinase 2 beta (EC 2.7.1.112) (Focal adhesion kinase 2) (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase beta) (CAK beta) (Calcium-dependent tyrosine kinase) (CADTK) (Related adhesion focal tyrosine kinase) [PTK2B] [Homo sapiens (Human)]** 1009 AA align

Score = 1914 bits (4957), Expect = 0.0
Identities = 958/1009 (94%), Positives = 958/1009 (94%)

```
Query: 1    MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
            MSGVSEPLSRVKLGTLRRPEGPA               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1    MSGVSEPLSRVKLGTLRRPEGPAEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
            CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
            LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
            LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS
Sbjct: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
            LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA
Sbjct: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300

Query: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
            EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG
Sbjct: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360

Query: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
            SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI
Sbjct: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420

Query: 421  AREDVVLNRILXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
            AREDVVLNRIL            TNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN
Sbjct: 421  AREDVVLNRILGEGFFGEVYEGVYTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480

Query: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
            LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL
Sbjct: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540

Query: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
            ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR
Sbjct: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600

Query: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
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Sbjct: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660

Query: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
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            CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQE
Sbjct: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEPPPKPSRP 720

Query: 721  XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                 QTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR
Sbjct: 721  KYRPPPQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780

Query: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
            EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP
Sbjct: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840

Query: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
            LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ
Sbjct: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900

Query: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
            LPPEGYVVVVKNVGLTLRKLIGSVDD          RTEIEGTQKLLNKDLAELINKMRLA
Sbjct: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDLLPSLPSSSRTEIEGTQKLLNKDLAELINKMRLA 960

Query: 961  QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
            QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE
Sbjct: 961  QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
```

tr Q6PID4 Q6PID4_HUMAN **PTK2B protein tyrosine kinase 2 beta, isoform a [PTK2B] [Homo sapiens (Human)]** 1009 AA align

```
 Score = 1912 bits (4954), Expect = 0.0
 Identities = 957/1009 (94%), Positives = 958/1009 (94%)

Query: 1    MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
             MSGVSEPLSRVKLGTLRRPEGPA               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1    MSGVSEPLSRVKLGTLRRPEGPAEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
             CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
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Sbjct: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
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Sbjct: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
             LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA
Sbjct: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300

Query: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
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Sbjct: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360

Query: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
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            SLTTHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI
Sbjct: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420

Query: 421  AREDVVLNRILXXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
            AREDVVLNRIL              TNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN
Sbjct: 421  AREDVVLNRILGEGFFGEVYEGVYTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480

Query: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
            LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL
Sbjct: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540

Query: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
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Sbjct: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600

Query: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
            RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR
Sbjct: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660

Query: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
            CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQE
Sbjct: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEPPPKPSRP 720

Query: 721  XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                  QTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR
Sbjct: 721  KYRPPPQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780

Query: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
            EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP
Sbjct: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840

Query: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
            LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ
Sbjct: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900

Query: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
            LPPEGYVVVVKNVGLTLRKLIGSVDD         RTEIEGTQKLLNKDLAELINKMRLA
Sbjct: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDLLPSLPSSSRTEIEGTQKLLNKDLAELINKMRLA 960

Query: 961  QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
            QQNAVTSLSEECKRQMLTASHTLA+DAKNLLDAVDQAKVLANLAHPPAE
Sbjct: 961  QQNAVTSLSEECKRQMLTASHTLAMDAKNLLDAVDQAKVLANLAHPPAE 1009
```

tr Q5R7F6 Q5R7F6_PONPY **Hypothetical protein DKFZp459L1823 [DKFZp459L1823] [Pongo pygmaeus (Orangutan)]** 1009 AA align

```
 Score = 1894 bits (4905), Expect = 0.0
 Identities = 948/1009 (93%), Positives = 953/1009 (93%)

Query: 1    MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
            MSGVSEPLSRVKLGTLRRPEGPA               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1    MSGVSEPLSRVKLGTLRRPEGPAEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
```

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            CTVQTEIREIITSILLSGRIGPNI+LAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61   CTVQTEIREIITSILLSGRIGPNIQLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
            LHVEAEWRYDLQIRYLPEDFMESLKEDPTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
            LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS
Sbjct: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
            LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA
Sbjct: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300

Query: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
            EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG
Sbjct: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360

Query: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
            SLIIHPRKDGEKRNSLPQIPMLNLEARRS LSESCSIESDIYAEIPDETLRR GGPQYGI
Sbjct: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSLLSESCSIESDIYAEIPDETLRRTGGPQYGI 420

Query: 421  AREDVVLNRILXXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
            AREDVVLNRIL             TNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN
Sbjct: 421  AREDVVLNRILGEGFFGEVYEGLYTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480

Query: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
            LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL
Sbjct: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540

Query: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
            ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR
Sbjct: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600

Query: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
            RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDL PPVLYTLMTR
Sbjct: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLFPPVLYTLMTR 660

Query: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
            CWDYDPSDRPRFTELVCSLSDVYQMEKDI MEQERNARYRTPKILEPT FQE
Sbjct: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIVMEQERNARYRTPKILEPTTFQEPPPKPSRP 720

Query: 721  XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                  QTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR
Sbjct: 721  KYRPPPQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780

Query: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
            EEDFI+PSSREEAQQLWEAEK+KMRQILDKQQKQMVEDYQWL+QEEKSLDPMVYMNDKSP
Sbjct: 781  EEDFIRPSSREEAQQLWEAEKIKMRQILDKQQKQMVEDYQWLKQEEKSLDPMVYMNDKSP 840

Query: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
            LTPEKEVGY+EFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ
Sbjct: 841  LTPEKEVGYMEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900

Query: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
            LPPEGYVVVVKNVGLTLRKLIGSVDD         RTEIEGTQKLLNKDLAELINKMRLA
Sbjct: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDLLPSLPSSSRTEIEGTQKLLNKDLAELINKMRLA 960
```

```
Query: 961   QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
             QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE
Sbjct: 961   QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
```

sp P70600 FAK2_RAT **Protein tyrosine kinase 2 beta (EC 2.7.1.112) (Focal adhesion kinase 2) (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase beta) (CAK beta) (Calcium-dependent tyrosine kinase) (CADTK) [Ptk2b] [Rattus norvegicus (Rat)]** 1009 AA align

Score = 1844 bits (4776), Expect = 0.0
Identities = 917/1009 (90%), Positives = 940/1009 (92%)

```
Query: 1     MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
              MSGVSEPLSRVK+GTLR PEGP               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1     MSGVSEPLSRVKVGTLRRPEGPPEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61    CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
              CTVQTEI+EIITSILLSGRIGPNI+LAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61    CTVQTEIQEIITSILLSGRIGPNIQLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121   LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
              LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121   LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181   LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
              LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS
Sbjct: 181   LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241   LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
              LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQD KPTCLA
Sbjct: 241   LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDTKPTCLA 300

Query: 301   EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
              EFKQIRSIRCLPLEE QAVLQLGIEGAPQ+LSIKTSSLAEAENMADLIDGYCRLQGEH+G
Sbjct: 301   EFKQIRSIRCLPLEETQAVLQLGIEGAPQSLSIKTSSLAEAENMADLIDGYCRLQGEHKG 360

Query: 361   SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
              SLIIH +KDGEKRNSLPQIP LNLE+RRSHLSESCSIESDIYAEIPDETLRRPGGPQYG+
Sbjct: 361   SLIIHAKKDGEKRNSLPQIPTLNLESRRSHLSESCSIESDIYAEIPDETLRRPGGPQYGV 420

Query: 421   AREDVVLNRILXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
              AREDVVLNRIL            TNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN
Sbjct: 421   AREDVVLNRILGEGFFGEVYEGVYTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480

Query: 481   LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
              LDHPHIVKLIGIIEEEPTWI+MELYPYGELGHYLERNKNSLKV TLVLY+LQICKAMAYL
Sbjct: 481   LDHPHIVKLIGIIEEEPTWIVMELYPYGELGHYLERNKNSLKVPTLVLYALQICKAMAYL 540

Query: 541   ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
              ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR
Sbjct: 541   ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
```

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Query: 601   RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
             RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKP+LCPPVLYTLMTR
Sbjct: 601   RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPELCPPVLYTLMTR 660

Query: 661   CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
             CWDYDPSDRPRFTELVCSLSD+YQME+DIA+EQERNARYR PKILEPTAFQE
Sbjct: 661   CWDYDPSDRPRFTELVCSLSDIYQMERDIAIEQERNARYRPPKILEPTAFQEPPPKPSRP 720

Query: 721   XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                   QTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR
Sbjct: 721   KYKHPPQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780

Query: 781   EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
             EEDFI+PSSREEAQQLWEAEK+KMRQ+LD+QQKQMVED QWLR+EE+ LDPMVYMNDKSP
Sbjct: 781   EEDFIRPSSREEAQQLWEAEKIKMRQVLDRQQKQMVEDSQWLRREERCLDPMVYMNDKSP 840

Query: 841   LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
             LTPEKE GY EFTGPPQKPPRLGAQSIQPTANLDRTDDLVY NVM LV AVLELKN+L Q
Sbjct: 841   LTPEKEAGYTEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYHNVMTLVEAVLELKNKLSQ 900

Query: 901   LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
             LPPE YVVVVKNVGL LRKLIGSVDD          RTEIEGTQKLLNKDLAELINKMRLA
Sbjct: 901   LPPEEYVVVVKNVGLNLRKLIGSVDDLLPSLPASSRTEIEGTQKLLNKDLAELINKMRLA 960

Query: 961   QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
             QQNAVTSLSE+CKRQMLTASHTLAVDAKNLLDAVDQAKV+ANLAHPPAE
Sbjct: 961   QQNAVTSLSEDCKRQMLTASHTLAVDAKNLLDAVDQAKVVANLAHPPAE 1009
```

sp Q9QVP9 FAK2_MOUSE **Protein tyrosine kinase 2 beta (EC 2.7.1.112) (Focal adhesion kinase 2) (FADK 2) (Proline-rich tyrosine kinase 2) (Cell adhesion kinase beta) (CAK beta) (Calcium-dependent tyrosine kinase) (CADTK) (Related adhesion focal tyrosine kinase) [Ptk2b] [Mus musculus (Mouse)]**

1009 AA align

```
 Score = 1838 bits (4761), Expect = 0.0
 Identities = 914/1009 (90%), Positives = 939/1009 (92%)

Query:. 1     MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
              MSGVSEPLSRVK+GTLRRPEGP                RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1      MSGVSEPLSRVKVGTLRRPEGPPEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61    CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
              CTVQTEI+EIITSILLSGRIGPNI+LAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61    CTVQTEIQEIITSILLSGRIGPNIQLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121   LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
              LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121   LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181   LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
              LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS
Sbjct: 181   LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241   LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
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            LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQD KPTCLA
Sbjct: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDTKPTCLA 300

Query: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
            EFKQIRSIRCLPLEE QAVLQLGIEGAPQ+LSIKTSSLAEAENMADLIDGYCRLQGEH+G
Sbjct: 301  EFKQIRSIRCLPLEETQAVLQLGIEGAPQSLSIKTSSLAEAENMADLIDGYCRLQGEHKG 360

Query: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
            SLI+H +KDGEKRNSLPQIP LNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYG+
Sbjct: 361  SLIMHAKKDGEKRNSLPQIPTLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGV 420

Query: 421  AREDVVLNRILXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
            ARE+VVLNRIL            TNHKGEKINVAVKTCKKDCT DNKEKFMSEAVIMKN
Sbjct: 421  AREEVVLNRILGEGFFGEVYEGVYTNHKGEKINVAVKTCKKDCTQDNKEKFMSEAVIMKN 480

Query: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
            LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKV TLVLY+LQICKAMAYL
Sbjct: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVPTLVLYTLQICKAMAYL 540

Query: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
            ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR
Sbjct: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600

Query: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
            RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKP+LCPPVLYTLMTR
Sbjct: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPELCPPVLYTLMTR 660

Query: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
            CWDYDPSDRPRFTELVCSLSD+YQMEKDIA+EQERNARYR PKILEPT FQE
Sbjct: 661  CWDYDPSDRPRFTELVCSLSDIYQMEKDIAIEQERNARYRPPKILEPTTFQEPPPKPSRP 720

Query: 721  XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                  QTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR
Sbjct: 721  KYRPPPQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780

Query: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
            EEDFI+PSSREEAQQLWEAEK+KM+Q+L++QQKQMVED QWLR+EE+ LDPMVYMNDKSP
Sbjct: 781  EEDFIRPSSREEAQQLWEAEKIKMKQVLERQQKQMVEDSQWLRREERCLDPMVYMNDKSP 840

Query: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
            LTPEKE GY EFTGPPQKPPRLGAQSIQPTANLDRTDDLVY NVM LV AVLELKN+L Q
Sbjct: 841  LTPEKEAGYTEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYHNVMTLVEAVLELKNKLGQ 900

Query: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
            LPPE YVVVVKNVGL LRKLIGSVDD         RTEIEGTQKLLNKDLAELINKM+LA
Sbjct: 901  LPPEDYVVVVKNVGLNLRKLIGSVDDLLPSLPASSRTEIEGTQKLLNKDLAELINKMKLA 960

Query: 961  QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
            QQNAVTSLSE+CKRQMLTASHTLAVDAKNLLDAVDQAKV+ANLAHPPAE
Sbjct: 961  QQNAVTSLSEDCKRQMLTASHTLAVDAKNLLDAVDQAKVVANLAHPPAE 1009
```

sp_vs Q14289-2 FAK2_HUMAN **Splice isoform 2 of Q14289 [PTK2B] [Homo sapiens (Human)]** 967 AA align

```
 Score = 1804 bits (4672), Expect = 0.0
 Identities = 916/1009 (90%), Positives = 916/1009 (90%), Gaps = 42/1009 (4%)

Query: 1    MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
            MSGVSEPLSRVKLGTLRRPEGPA               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1    MSGVSEPLSRVKLGTLRRPEGPAEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
            CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
            LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
            LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS
Sbjct: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
            LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA
Sbjct: 241  LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300

Query: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
            EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG
Sbjct: 301  EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360

Query: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
            SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI
Sbjct: 361  SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420

Query: 421  AREDVVLNRILXXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
            AREDVVLNRIL             TNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN
Sbjct: 421  AREDVVLNRILGEGFFGEVYEGVYTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480

Query: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
            LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL
Sbjct: 481  LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540

Query: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
            ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR
Sbjct: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600

Query: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
            RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR
Sbjct: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660

Query: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
            CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQE
Sbjct: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEPPPKPSRP 720

Query: 721  XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                  QTNLLAPKLQFQ
Sbjct: 721  KYRPPPQTNLLAPKLQFQ---------------------------------------- 738

Query: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
            EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP
Sbjct: 739  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 798
```

```
Query: 841   LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
             LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ
Sbjct: 799   LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 858

Query: 901   LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
             LPPEGYVVVVKNVGLTLRKLIGSVDD          RTEIEGTQKLLNKDLAELINKMRLA
Sbjct: 859   LPPEGYVVVVKNVGLTLRKLIGSVDDLLPSLPSSSRTEIEGTQKLLNKDLAELINKMRLA 918

Query: 961   QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
             QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE
Sbjct: 919   QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 967
```

sp_vs P70600-3 FAK2_RAT **Splice isoform 3 of P70600 [Ptk2b] [Rattus norvegicus (Rat)]** 967 AA align

```
 Score = 1734 bits (4491), Expect = 0.0
 Identities = 875/1009 (86%), Positives = 898/1009 (88%), Gaps = 42/1009 (4%)

Query: 1     MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
              MSGVSEPLSRVK+GTLR PEGP               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1     MSGVSEPLSRVKVGTLRRPEGPPEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61    CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
              CTVQTEI+EIITSILLSGRIGPNI+LAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61    CTVQTEIQEIITSILLSGRIGPNIQLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121   LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
              LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121   LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181   LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
              LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS
Sbjct: 181   LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240

Query: 241   LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDAKPTCLA 300
              LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQD KPTCLA
Sbjct: 241   LREEECVMKFFNTLAGFANIDQETYRCELIQGWNITVDLVIGPKGIRQLTSQDTKPTCLA 300

Query: 301   EFKQIRSIRCLPLEEGQAVLQLGIEGAPQALSIKTSSLAEAENMADLIDGYCRLQGEHQG 360
              EFKQIRSIRCLPLEE QAVLQLGIEGAPQ+LSIKTSSLAEAENMADLIDGYCRLQGEH+G
Sbjct: 301   EFKQIRSIRCLPLEETQAVLQLGIEGAPQSLSIKTSSLAEAENMADLIDGYCRLQGEHKG 360

Query: 361   SLIIHPRKDGEKRNSLPQIPMLNLEARRSHLSESCSIESDIYAEIPDETLRRPGGPQYGI 420
              SLIIH +KDGEKRNSLPQIP LNLE+RRSHLSESCSIESDIYAEIPDETLRRPGGPQYG+
Sbjct: 361   SLIIHAKKDGEKRNSLPQIPTLNLESRRSHLSESCSIESDIYAEIPDETLRRPGGPQYGV 420

Query: 421   AREDVVLNRILXXXXXXXXXXXXTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480
              AREDVVLNRIL            TNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN
Sbjct: 421   AREDVVLNRILGEGFFGEVYEGVYTNHKGEKINVAVKTCKKDCTLDNKEKFMSEAVIMKN 480

Query: 481   LDHPHIVKLIGIIEEEPTWIIMELYPYGELGHYLERNKNSLKVLTLVLYSLQICKAMAYL 540
              LDHPHIVKLIGIIEEEPTWI+MELYPYGELGHYLERNKNSLKV TLVLY+LQICKAMAYL
Sbjct: 481   LDHPHIVKLIGIIEEEPTWIVMELYPYGELGHYLERNKNSLKVPTLVLYALQICKAMAYL 540
```

```
Query: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600
            ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR
Sbjct: 541  ESINCVHRDIAVRNILVASPECVKLGDFGLSRYIEDEDYYKASVTRLPIKWMSPESINFR 600

Query: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPDLCPPVLYTLMTR 660
            RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKP+LCPPVLYTLMTR
Sbjct: 601  RFTTASDVWMFAVCMWEILSFGKQPFFWLENKDVIGVLEKGDRLPKPELCPPVLYTLMTR 660

Query: 661  CWDYDPSDRPRFTELVCSLSDVYQMEKDIAMEQERNARYRTPKILEPTAFQEXXXXXXXX 720
            CWDYDPSDRPRFTELVCSLSD+YQME+DIA+EQERNARYR PKILEPTAFQE
Sbjct: 661  CWDYDPSDRPRFTELVCSLSDIYQMERDIAIEQERNARYRPPKILEPTAFQEPPPKPSRP 720

Query: 721  XXXXXXQTNLLAPKLQFQVPEGLCASSPTLTSPMEYPSPVNSLHTPPLHRHNVFKRHSMR 780
                  QTNLLAPKLQFQ
Sbjct: 721  KYKHPPQTNLLAPKLQFQ---------------------------------------- 738

Query: 781  EEDFIQPSSREEAQQLWEAEKVKMRQILDKQQKQMVEDYQWLRQEEKSLDPMVYMNDKSP 840
            EEDFI+PSSREEAQQLWEAEK+KMRQ+LD+QQKQMVED QWLR+EE+ LDPMVYMNDKSP
Sbjct: 739  EEDFIRPSSREEAQQLWEAEKIKMRQVLDRQQKQMVEDSQWLRREERCLDPMVYMNDKSP 798

Query: 841  LTPEKEVGYLEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYLNVMELVRAVLELKNELCQ 900
            LTPEKE GY EFTGPPQKPPRLGAQSIQPTANLDRTDDLVY NVM LV AVLELKN+L Q
Sbjct: 799  LTPEKEAGYTEFTGPPQKPPRLGAQSIQPTANLDRTDDLVYHNVMTLVEAVLELKNKLSQ 858

Query: 901  LPPEGYVVVVKNVGLTLRKLIGSVDDXXXXXXXXXRTEIEGTQKLLNKDLAELINKMRLA 960
            LPPE YVVVVKNVGL LRKLIGSVDD         RTEIEGTQKLLNKDLAELINKMRLA
Sbjct: 859  LPPEEYVVVVKNVGLNLRKLIGSVDDLLPSLPASSRTEIEGTQKLLNKDLAELINKMRLA 918

Query: 961  QQNAVTSLSEECKRQMLTASHTLAVDAKNLLDAVDQAKVLANLAHPPAE 1009
            QQNAVTSLSE+CKRQMLTASHTLAVDAKNLLDAVDQAKV+ANLAHPPAE
Sbjct: 919  QQNAVTSLSEDCKRQMLTASHTLAVDAKNLLDAVDQAKVVANLAHPPAE 967
```

tr Q8C2G0 Q8C2G0_MOUSE **Mus musculus 2 days neonate thymus thymic cells cDNA, RIKEN full-length enriched library, clone:E430023O05 product:protein tyrosine kinase 2 beta, full insert sequence [Ptk2b] [Mus musculus (Mouse)]**

967 AA align

```
 Score = 1727 bits (4473), Expect = 0.0
 Identities = 871/1009 (86%), Positives = 897/1009 (88%), Gaps = 42/1009 (4%)

Query: 1    MSGVSEPLSRVKLGTLRRPEGPAXXXXXXXXXXXXXXXRILKVCFYSNSFNPGKNFKLVK 60
            MSGVSEPLSRVK+GTLRRPEGP               RILKVCFYSNSFNPGKNFKLVK
Sbjct: 1    MSGVSEPLSRVKVGTLRRPEGPPEPMVVVPVDVEKEDVRILKVCFYSNSFNPGKNFKLVK 60

Query: 61   CTVQTEIREIITSILLSGRIGPNIRLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120
            CTVQTEI+EIITSILLSGRIGPNI+LAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC
Sbjct: 61   CTVQTEIQEIITSILLSGRIGPNIQLAECYGLRLKHMKSDEIHWLHPQMTVGEVQDKYEC 120

Query: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180
            LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC
Sbjct: 121  LHVEAEWRYDLQIRYLPEDFMESLKEDRTTLLYFYQQLRNDYMQRYASKVSEGMALQLGC 180

Query: 181  LELRRFFKDMPHNALDKKSNFELLEKEVGLDLFFPKQMQENLKPKQFRKMIQQTFQQYAS 240
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Welcome to the SIB BLAST Network Service

If results of this search are reported or published, please mention that the computation was performed at the SIB using the BLAST network service. The SIB BLAST network service uses a server developed at SIB and the NCBI BLAST 2 software.

In case of problems, please read the online BLAST help.
If your question is not covered, please contact <helpdesk@expasy.org>.

NCBI BLAST program reference [PMID:9254694]:
Altschul S.F., Madden T.L., Schäffer A.A., Zhang J., Zhang Z., Miller W., Lipman D.J. Gapped BLAST and PSI-BLAST: a new generation of protein database search programs. Nucleic Acids Res. 25:3389-3402(1997).

==========

Query: 1187 AA (of which 2% low-complexity regions filtered out)
Date run: 2005-08-10 10:18:51 UTC+0100 on sib-gm1.unil.ch
Program: NCBI BLASTP 1.5.4-Paracel [2003-06-05]
Database: EXPASY/UniProtKB
2,142,762 sequences; 699,641,365 total letters
UniProt Knowledgebase Release 5.6 consists of:
UniProtKB/Swiss-Prot Release 47.6 of 02-Aug-2005: 188752 entries
UniProtKB/TrEMBL Release 30.6 of 02-Aug-2005: 1942311 entries

Taxonomic view | NiceBlast view | Printable view

List of potentially matching sequences

Send selected sequences to Clustal W (multiple alignment) Submit Query
Select up to...

☐ Include query sequence

	Db	AC	Description	Score	E-va
☐	sp	P29597	TYK2_HUMAN Non-receptor tyrosine-protein kinase TYK2 (...	2395	
☐	tr	Q684M7	_PIG Tyrosine kinase 2 [TYK2] [Sus scrofa (Pig)]	1960	
☐	sp	Q9R117	TYK2_MOUSE Non-receptor tyrosine-protein kinase TYK2 (...	1875	
☐	tr	Q52KQ2	_MOUSE Tyrosine kinase 2 [Tyk2] [Mus musculus (Mouse)]	1871	
☐	tr	Q53HA9	_HUMAN Tyrosine kinase 2 variant (Fragment) [Homo sapie...	1655	
☐	tr	Q6GPK5	_XENLA MGC83617 protein [MGC83617] [Xenopus laevis (Afr...	1345	
☐	tr	Q9PWM9	_CHICK Tyrosine kinase JAK1 [JAK1] [Gallus gallus (Chic...	984	
☐	tr	Q6DDJ0	_XENLA Jak1-prov protein [jak1-prov] [Xenopus laevis (A...	954	
☐	sp	P52332	JAK1_MOUSE Tyrosine-protein kinase JAK1 (EC 2.7.1.112)...	952	

tr	Q9TTJ1	_PIG Janus kinase 1 [JAK1] [Sus scrofa (Pig)]	952	
tr	Q59GQ2	_HUMAN Janus kinase 1 variant (Fragment) [janus kinase ...	950	
tr	Q9PWD1	_TETFL TYK2 tyrosine kinase [TYK2] [Tetraodon fluviatil...	947	
sp	P23458	JAK1_HUMAN Tyrosine-protein kinase JAK1 (EC 2.7.1.112)...	946	
sp	O12990	JAK1_BRARE Tyrosine-protein kinase Jak1 (EC 2.7.1.112)...	934	
tr	Q7ZU16	_BRARE Janus kinase 1 [jak1] [Brachydanio rerio (Zebraf...	933	
tr	Q4LDX3	_HUMAN Janus kinase 1 [JAK1] [Homo sapiens (Human)]	929	
tr	O57612	_TETFL JAK1 tyrosine kinase [JAK1] [Tetraodon fluviatil...	928	
tr	Q4RJ39	_TETNG Chromosome 1 SCAF15039, whole genome shotgun seq...	921	
sp	Q09178	JAK1_CYPCA Tyrosine-protein kinase Jak1 (EC 2.7.1.112)...	878	
tr	O62756	_PIG Non-receptor tyrosine kinase JAK1 (Fragment) [Jak1...	838	
sp	Q62689	JAK2_RAT Tyrosine-protein kinase JAK2 (EC 2.7.1.112) (...	728	
tr	Q7TQD0	_MOUSE Jak2 protein [Jak2] [Mus musculus (Mouse)]	728	
sp	Q62120	JAK2_MOUSE Tyrosine-protein kinase JAK2 (EC 2.7.1.112)...	727	
tr	Q75R65	_CHICK Tyrosine kinase [JAK-2] [Gallus gallus (Chicken)]	724	
tr	O19064	_PIG JAK2 [Sus scrofa (Pig)]	721	
sp	O60674	JAK2_HUMAN Tyrosine-protein kinase JAK2 (EC 2.7.1.112)...	720	
tr	Q5RB23	_PONPY Hypothetical protein DKFZp469G074 [DKFZp469G074]...	720	
tr	Q8IXP2	_HUMAN JAK2 protein [Homo sapiens (Human)]	720	
tr	Q506Q0	_HUMAN Janus kinase 2 [JAK2] [Homo sapiens (Human)]	718	
tr	O93596	_BRARE Protein tyrosine kinase (EC 2.7.1.112) [jak2a] [...	712	
tr	Q6Y4Q0	_TETFL Tyrosine kinase jak2b [Tetraodon fluviatilis (Pu...	710	
tr	Q9PVI2	_TETFL Jak2 tyrosine kinase [JAK2] [Tetraodon fluviatil...	696	
tr	O42291	_CHICK Janus tyrosine kinase [JAK] [Gallus gallus (Chic...	682	
tr	O35803	_RAT Janus protein tyrosine kinase 1 (Fragment) [JAK1] ...	682	
tr	Q9TTI9	_PIG Kinase-defective JAK2 variant [JAK2] [Sus scrofa (...	678	
sp	P52333	JAK3_HUMAN Tyrosine-protein kinase JAK3 (EC 2.7.1.112)...	676	
tr	Q99699	_HUMAN JAK3 [JAK3] [Homo sapiens (Human)]	669	
tr	Q6GP63	_XENLA LOC443637 protein (Fragment) [LOC443637] [Xenopu...	667	
tr	Q8K0I7	_MOUSE Jak1 protein [Jak1] [Mus musculus (Mouse)]	665	
tr	Q8BYU2	_MOUSE Mus musculus 16 days neonate thymus cDNA, RIKEN ...	659	
sp_vs	P52333-2	Splice isoform 1 of P52333 [JAK3] [Homo sapiens (...	655	
sp_vs	P52333-3	Splice isoform 3 of P52333 [JAK3] [Homo sapiens (...	655	
tr	Q8BTY6	_MOUSE Mus musculus 2 days neonate thymus thymic cells ...	655	
tr	Q9PTN6	_CYPCA Janus kinase 3 [Cyprinus carpio (Common carp)]	650	
sp	Q63272	JAK3_RAT Tyrosine-protein kinase JAK3 (EC 2.7.1.112) (...	644	
sp_vs	Q62137-3	Splice isoform 3 of Q62137 [Jak3] [Mus musculus (...	640	
sp_vs	Q62137-2	Splice isoform 2 of Q62137 [Jak3] [Mus musculus (...	633	e-
tr	Q9PWD0	_TETFL JAK3 tyrosine kinase [JAK3] [Tetraodon fluviatil...	627	e-
tr	Q4SFG7	_TETNG Chromosome 1 SCAF14603, whole genome shotgun seq...	620	e-
tr	P97423	_MOUSE JAK3 [Jak3] [Mus musculus (Mouse)]	619	e-
tr	O97892	_PIG Non-receptor tyrosine kinase Tyk2 (Fragment) [Sus ...	595	e-
sp	Q62137	JAK3_MOUSE Tyrosine-protein kinase JAK3 (EC 2.7.1.112)...	535	e-
tr	Q6W5B1	_BRARE TEL/JAK2 fusion protein [Brachydanio rerio (Zebr...	518	e-
tr	Q4T1R9	_TETNG Chromosome 4 SCAF10492, whole genome shotgun seq...	507	e-

☐	tr	Q9TTJ0	_PIG Kinase-defective JAK2 variant [JAK2] [Sus scrofa (...	448 e-
☐	tr	O93597	_BRARE Protein tyrosine kinase (EC 2.7.1.112) (Fragment...	439 e-
☐	tr	O35804	_RAT Janus protein tyrosine kinase 2 (Fragment) [Jak2] ...	391 e-
☐	tr	Q4RHE1	_TETNG Chromosome 3 SCAF15050, whole genome shotgun seq...	352 4e
☐	tr	Q9N143	_MACMU Tyrosine kinase-2 (Fragment) [Tyk2] [Macaca mula...	347 8e
☐	tr	Q4RHE2	_TETNG Chromosome 3 SCAF15050, whole genome shotgun seq...	324 8e
☐	tr	Q4RU24	_TETNG Chromosome 12 SCAF14996, whole genome shotgun se...	318 4e
☐	tr	Q4TGV3	_TETNG Chromosome undetermined SCAF3451, whole genome s...	258 5e
☐	tr	Q8N1E8	_HUMAN JAK3 protein [Homo sapiens (Human)]	245 4e
☐	tr	Q5FVF5	_RAT Jak1 protein [Jak1] [Rattus norvegicus (Rat)]	228 6e
☐	tr	Q6JDV3	_PIG Tyrosine kinase 2 (Fragment) [TYK2] [Sus scrofa (P...	221 9e
☐	tr	Q4TGU3	_TETNG Chromosome undetermined SCAF3474, whole genome s...	175 6e
☐	tr	Q7Q4D9	_ANOGA ENSANGP00000019506 (Fragment) [ENSANGG0000001701...	174 1e
☐	tr	Q8CFX4	_MOUSE Jak1 protein (Fragment) [Jak1] [Mus musculus (Mo...	169 4e
☐	tr	O77440	_HYDAT Protein-tyrosine kinase HTK98 [HTK98] [Hydra att...	168 9e
☐	sp	P24786	NTRK3_PIG NT-3 growth factor receptor precursor (EC 2....	167 1e
☐	sp	Q91044	NTRK3_CHICK NT-3 growth factor receptor precursor (EC ...	167 2e
☐	sp	Q5IS37	NTRK3_PANTR NT-3 growth factor receptor precursor (EC ...	164 1e
☐	sp	Q5IFJ9	NTRK3_MACFA NT-3 growth factor receptor precursor (EC ...	164 1e
☐	tr	Q6VNS1	_MOUSE Neurotrophic tyrosine kinase receptor [Ntrk3] [M...	164 1e
☐	sp_vs	Q16288-3	Splice isoform C of Q16288 [NTRK3] [Homo sapiens ...	164 1e
☐	sp_vs	Q03351-2	Splice isoform TRKC of Q03351 [Ntrk3] [Rattus nor...	164 1e
☐	tr	Q5IS82	_9PRIM Neurotrophic tyrosine kinase receptor type 3 [Sa...	162 5e
☐	sp	Q63604	NTRK2_RAT BDNF/NT-3 growth factors receptor precursor ...	162 7e
☐	sp	O54967	ACK1_MOUSE Activated CDC42 kinase 1 (EC 2.7.1.112) (AC...	161 1e
☐	sp	Q07912	ACK1_HUMAN Activated CDC42 kinase 1 (EC 2.7.1.112) (AC...	161 1e
☐	tr	Q6ZMQ0	_HUMAN Hypothetical protein FLJ16772 [Homo sapiens (Hum...	161 1e
☐	sp_vs	Q07912-2	Splice isoform 2 of Q07912 [TNK2] [Homo sapiens (...	161 1e
☐	sp_vs	O54967-2	Splice isoform 2 of O54967 [Tnk2] [Mus musculus (...	161 1e
☐	sp_vs	O54967-3	Splice isoform 3 of O54967 [Tnk2] [Mus musculus (...	161 1e
☐	sp	P35739	NTRK1_RAT High affinity nerve growth factor receptor p...	160 1e
☐	sp_vs	P35739-2	Splice isoform TrkA-I of P35739 [Ntrk1] [Rattus n...	160 1e
☐	sp	Q16620	NTRK2_HUMAN BDNF/NT-3 growth factors receptor precurso...	160 2e
☐	sp	O02742	ACK2_BOVIN Activated CDC42 kinase 2 (EC 2.7.1.112) (AC...	160 2e
☐	tr	Q5VVP4	_HUMAN Neurotrophic tyrosine kinase, receptor, type 2 [...	160 2e
☐	tr	Q8WXJ7	_HUMAN Neurotrophin receptor tyrosine kinase type 2 (Ne...	160 2e
☐	sp	P15209	NTRK2_MOUSE BDNF/NT-3 growth factors receptor precurso...	160 2e
☐	sp_vs	P15209-3	Splice isoform L1 of P15209 [Ntrk2] [Mus musculus...	160 2e
☐	sp_vs	P15209-4	Splice isoform L10 of P15209 [Ntrk2] [Mus musculu...	160 2e
☐	sp	Q91987	NTRK2_CHICK BDNF/NT-3 growth factors receptor precurso...	159 4e
☐	tr	Q6B515	_POEGU Tyrosine kinase receptor (Fragment) [Poephila gu...	159 4e
☐	sp_vs	Q91987-2	Splice isoform 2 of Q91987 [NTRK2] [Gallus gallus...	159 4e
☐	sp_vs	Q91987-3	Splice isoform 3 of Q91987 [NTRK2] [Gallus gallus...	159 4e
☐	sp_vs	Q91987-4	Splice isoform 4 of Q91987 [NTRK2] [Gallus gallus...	159 4e
☐	sp_vs	Q91987-5	Splice isoform 5 of Q91987 [NTRK2] [Gallus gallus...	159 4e

☐ tr Q9YH44 _XENLA Neurotrophin receptor B xTrkB-alpha [xTrkB] [Xen... 159 6e

Graphical overview of the alignments

Click here to resubmit your query after masking regions matching PROSITE profiles or Pfam HMMs

(Help) (use ScanProsite for more details about PROSITE matches)


Matches on query sequence
Mat
Submission
1
500
1000
1
TYK2_HUMAN
Q684M7
TYK2_MOUSE
Q52KQ2
Q53HA9
Q6GPK5
Q9PWM9
Q6DDJ0
JAK1_MOUSE
Q9TTJ1
Q59GQ2
Q9PWD1
JAK1_HUMAN
JAK1_BRARE
Q7ZU16
Q4LDX3
O57612
Q4RJ39
JAK1_CYPCA
O62756
JAK2_RAT
Q7TQD0
JAK2_MOUSE
Q75R65
O19064
JAK2_HUMAN
Q5RB23
Q8IXP2
Q506Q0
O93596
Q6Y4Q0
Q9PVI2
O42291
O35803
Q9TTI9
JAK3_HUMAN
Q99699
Q6GP63
Q8K0I7
Q8BYU2
JAK3_HUMAN-2
JAK3_HUMAN-3
Q8BTY6
Q9PTN6
JAK3_RAT
JAK3_MOUSE-3
JAK3_MOUSE-2
Q9PWD0
Q4SFG7
P97423
O97892
JAK3_MOUSE
Q6W5B1
Q4T1R9
Q9TTJ0
O93597
O35804
Q4RHE1
Q9N143
Q4RHE2
Q4RU24
Q4TGV3
Q8N1E8
Q5FVF5
Q6JDV3
Q4TGU3
Q7Q4D9
Q8CFX4
O77440
NTRK3_PIG
NTRK3_CHICK
NTRK3_PANTR
NTRK3_MACFA
Q6VNS1
NTRK3_HUMAN-3
NTRK3_RAT-2
Q5IS82
NTRK2_RAT
ACK1_MOUSE
ACK1_HUMAN
Q6ZM00
ACK1_HUMAN-2
ACK1_MOUSE-2
ACK1_MOUSE-3
NTRK1_RAT
NTRK1_RAT-2

Alignments

sp P29597 TYK2_HUMAN **Non-receptor tyrosine-protein kinase TYK2 (EC 2.7.1.112) [TYK2] [Homo sapiens (Human)]** 1187 AA align

Score = 2395 bits (6206), Expect = 0.0
Identities = 1159/1187 (97%), Positives = 1159/1187 (97%)

```
Query: 1    MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHI 60
            MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHI
Sbjct: 1    MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHI 60

Query: 61   AHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREP 120
            AHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREP
Sbjct: 61   AHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREP 120

Query: 121  AVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFK 180
            AVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFK
Sbjct: 121  AVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFK 180

Query: 181  NESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTXXXXXXXXXX 240
            NESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALT
Sbjct: 181  NESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTRLRLRNVFRR 240

Query: 241  XXXXXQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAP 300
                 QPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAP
Sbjct: 241  FLRDFQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAP 300

Query: 301  TDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHK 360
            TDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHK
Sbjct: 301  TDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHK 360

Query: 361  AVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLV 420
            AVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLV
Sbjct: 361  AVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLV 420

Query: 421  DGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHP 480
            DGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHP
Sbjct: 421  DGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHP 480

Query: 481  YRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRA 540
            YRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRA
Sbjct: 481  YRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRA 540

Query: 541  GDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTR 600
            GDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTR
Sbjct: 541  GDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTR 600

Query: 601  TNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETAS 660
            TNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETAS
Sbjct: 601  TNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETAS 660

Query: 661  LMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLAS 720
            LMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLAS
Sbjct: 661  LMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLAS 720
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Query: 721  ALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLA 780
            ALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLA
Sbjct: 721  ALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLA 780

Query: 781  PECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCPQ 840
            PECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCPQ
Sbjct: 781  PECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCPQ 840

Query: 841  LATLTSQCLTYEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKKI 900
            LATLTSQCLTYEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKKI
Sbjct: 841  LATLTSQCLTYEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKKI 900

Query: 901  RDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHII 960
            RDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHII
Sbjct: 901  RDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHII 960

Query: 961  KYKGCCEDQGEKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHYI 1020
            KYKGCCEDQGEKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHYI
Sbjct: 961  KYKGCCEDQGEKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHYI 1020

Query: 1021 HRDLAARNVLLDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFYY 1080
            HRDLAARNVLLDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFYY
Sbjct: 1021 HRDLAARNVLLDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFYY 1080

Query: 1081 ASDVWSFGVTLYELLTHCDSSQSPPTKFLELIGIAQGQMTVXXXXXXXXXXXXXPRPDKC 1140
            ASDVWSFGVTLYELLTHCDSSQSPPTKFLELIGIAQGQMTV             PRPDKC
Sbjct: 1081 ASDVWSFGVTLYELLTHCDSSQSPPTKFLELIGIAQGQMTVLRLTELLERGERLPRPDKC 1140

Query: 1141 PCEVYHLMKNCWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC 1187
            PCEVYHLMKNCWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC
Sbjct: 1141 PCEVYHLMKNCWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC 1187
```

tr Q684M7 **Tyrosine kinase 2 [TYK2] [Sus scrofa (Pig)]** 1184 AA
Q684M7_PIG align

```
 Score = 1960 bits (5077), Expect = 0.0
 Identities = 962/1188 (80%), Positives = 1029/1188 (85%), Gaps = 5/1188 (0%)

Query: 1    MPLRHWGMA-RGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIH 59
            MPL HWG   RG KP GDGAQP A   GLKVLLHWAGPGGGEPWVTFSE +LTAEEVCIH
Sbjct: 1    MPLCHWGATTRGRKPDGDGAQPTATTEGLKVLLHWAGPGGGEPWVTFSEVTLTAEEVCIH 60

Query: 60   IAHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPRE 119
            IAH+VGI+P C NLFALFDAQAQVWLPPNHIL+I  D+SL L+FR+RFYFRNWHGMNP+E
Sbjct: 61   IAHRVGISPLCLNLFALFDAQAQVWLPPNHILDISGDSSLTLHFRMRFYFRNWHGMNPQE 120

Query: 120  PAVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHF 179
            PAVYRCGPPGTE +S+Q   G+QLLDPASFEYLFEQGKHEFVNDVASLWELS+EEEIHHF
Sbjct: 121  PAVYRCGPPGTE-TSEQAEPGVQLLDPASFEYLFEQGKHEFVNDVASLWELSSEEEIHHF 179

Query: 180  KNESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTXXXXXXXXX 239
            +NESLGMAFLHLC LALRHG+PLE+VAKK SFKDCIPRSFRR IRQH+ALT
Sbjct: 180  QNESLGMAFLHLCQLALRHGVPLEKVAKKISFKDCIPRSFRRQIRQHNALTRLRLRSIFR 239

Query: 240  XXXXXXQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVA 299
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                QPG LSQQ+VMVKYLATLERLAPRFGTERVPVC L+LLAQAEGEPCYIRD G +
Sbjct: 240  KFLRAFQPGCLSQQVVMVKYLATLERLAPRFGTERVPVCRLQLLAQAEGEPCYIRDGGQS 299

Query: 300  PTDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAH 359
               DP P++A  P THEVLV+GT GIQW  V+ E        GSS R+P     GKKAKA
Sbjct: 300  SPDPEPQAAPEPTTHEVLVSGTDGIQWRLVQAEGPSGGAGDGSSSRSPHTGHSGKKAKAQ 359

Query: 360  KAVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSL 419
             +   QP DRP E LW YFC+F+DITHVVLKE  VSIH QD KCLEL+LPSRA ALS V+L
Sbjct: 360  ERGNQPVDRPGEALWTYFCNFQDITHVVLKERHVSIHCQD-KCLELTLPSRATALSLVAL 418

Query: 420  VDGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSH 479
             VDGYFRLTADSSHYLCHEVAPPRLVMSI+DGIHGPLLEPFV AKLRPEDGLYLIHWSTSH
Sbjct: 419  VDGYFRLTADSSHYLCHEVAPPRLVMSIQDGIHGPLLEPFVLAKLRPEDGLYLIHWSTSH 478

Query: 480  PYRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLR 539
               RLILTVAQR QAP G + LRLRKFPIE Q      LEGWGRSFPSVREL AALQGC LR
Sbjct: 479  LNRLILTVAQRDQAP-GTKGLRLRKFPIELQAETVTLEGWGRSFPSVRELRAALQGCSLR 537

Query: 540  AGDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGT 599
             AGDDCFSL RCCLP+PGE SNLIT RG +A  R LNLS LSFHRV Q++ITQLSHLGQGT
Sbjct: 538  AGDDCFSLDRCCLPRPGEISNLIITRGPQACTRPLNLSHLSFHRVHQEDITQLSHLGQGT 597

Query: 600  RTNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETA 659
             RTNVYEG LRV G G PEE K D  DP      DRGQELRVVLKVLDPSHHDIALAFYETA
Sbjct: 598  RTNVYEGLLRV-GGGGPEEEKSDGRDPSPSSGDRGQELRVVLKVLDPSHHDIALAFYETA 656

Query: 660  SLMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLA 719
             SLMSQVSH HL FVHGV V G ENIMVTEYVEHGPLDVWLRRERGHVP+AWK+ VAQQLA
Sbjct: 657  SLMSQVSHVHLVFVHGVYVHGSENIMVTEYVEHGPLDVWLRRERGHVPLAWKLAVAQQLA 716

Query: 720  SALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWL 779
             SALSYLE+K+LVHGNVCGRNILLARLG AEGTSPFIKLSDPGVGL ALSREERVERIPW
Sbjct: 717  SALSYLEDKSLVHGNVCGRNILLARLGQAEGTSPFIKLSDPGVGLNALSREERVERIPWT 776

Query: 780  APECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCP 839
             APECL GGANSLSTA DKWGFGATLLEICFDGEAPLQ R PSEKE FYQ+QH+LPEPSCP
Sbjct: 777  APECLSGGANSLSTAADKWGFGATLLEICFDGEAPLQGRGPSEKERFYQKQHKLPEPSCP 836

Query: 840  QLATLTSQCLTYEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKK 899
             +LATLTSQCLTYEP QRPSFRTILRDLT+LQP NLADVL+VNPD P SDPT+FHKRYLKK
Sbjct: 837  ELATLTSQCLTYEPAQRPSFRTILRDLTQLQPQNLADVLSVNPDLPTSDPTIFHKRYLKK 896

Query: 900  IRDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHI 959
             IRDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKA CG Q R+GW++EIDILRTLYHEHI
Sbjct: 897  IRDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKAGCGSQLRTGWRREIDILRTLYHEHI 956

Query: 960  IKYKGCCEDQGEKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHY 1019
             +KYKGCCEDQGEKS+QLVMEYVPLGSLRDYLPR ++GLAQLLLFAQQICEGMAYLHAQHY
Sbjct: 957  VKYKGCCEDQGEKSVQLVMEYVPLGSLRDYLPRQNVGLAQLLLFAQQICEGMAYLHAQHY 1016

Query: 1020 IHRDLAARNVLLDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFY 1079
             +RDLAARNVLLDN+RLVKIGDFGLAKAVPEGH+YY VREDGDSPVFWYAPECLKE KFY
Sbjct: 1017 VHRDLAARNVLLDNNRLVKIGDFGLAKAVPEGHDYYCVREDGDSPVFWYAPECLKECKFY 1076

Query: 1080 YASDVWSFGVTLYELLTHCDSSQSPPTKFLELIGIAQGQMTVXXXXXXXXXXXXPRPDK 1139
             YASDVWSFGVT+YELLT+CDSSQSPP+KF+ELIG+ QGQMTV              P+P+K
Sbjct: 1077 YASDVWSFGVTMYELLTYCDSSQSPPSKFIELIGLTQGQMTVLRLTELLEQGERLPQPEK 1136
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Query: 1140 CPCEVYHLMKNCWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC 1187
            CP E+Y LMKNCWE +ASFRPTF+NL+PILKT+ EKYQGQAPSVFSVC
Sbjct: 1137 CPHEIYRLMKNCWEAKASFRPTFQNLVPILKTIQEKYQGQAPSVFSVC 1184
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sp Q9R117 TYK2_MOUSE **Non-receptor tyrosine-protein kinase TYK2 (EC 2.7.1.112) [Tyk2] [Mus musculus (Mouse)]** 1180 AA align

```
 Score = 1875 bits (4856), Expect = 0.0
 Identities = 915/1177 (77%), Positives = 999/1177 (84%), Gaps = 10/1177 (0%)

Query: 12   SKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHIAHKVGITPPCF 71
            SK  G  AQP+   G L VLLHW GP GGEPWVTFS++SLTAEEVCIHIAHKVGITPPC
Sbjct: 13   SKADGTEAQPLVPTGCLMVLLHWPGPEGGEPWVTFSQTSLTAEEVCIHIAHKVGITPPCL 72

Query: 72   NLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREPAVYRCGPPGTE 131
            NLFAL++AQA+VWLPPNHIL+  +D +L  YFR+RFYFRNWHGMNP+EPAVYRCG PG E
Sbjct: 73   NLFALYNAQAKVWLPPNHILDTSQDMNL--YFRMRFYFRNWHGMNPQEPAVYRCGFPGAE 130

Query: 132  ASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFKNESLGMAFLHL 191
             SSD+  QG+QLLD ASFEYLFEQGKHEF+NDV SL +LS+EEEIHHFKNESLGMAFLHL
Sbjct: 131  TSSDRAEQGVQLLDSASFEYLFEQGKHEFMNDVVSLRDLSSEEEIHHFKNESLGMAFLHL 190

Query: 192  CHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTXXXXXXXXXXXXXXQPGRLS 251
            CHLAL  G+PLEE+A++ SFK+CIP SFR+HIRQH+ LT              +PG LS
Sbjct: 191  CHLALSRGVPLEEMAREISFKNCIPHSFRQHIRQHNVLTRLRLHRVFRRFLRAFRPGHLS 250

Query: 252  QQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAPTDPGPESAAGP 311
            QQ+VMVKYLATLERLAPRFG+ER+PVCHL +LAQ E +PCYI++SG    DPGPE  +GP
Sbjct: 251  QQVVMVKYLATLERLAPRFGSERIPVCHLEVLAQPERDPCYIQNSGQTAGDPGPELPSGP 310

Query: 312  PTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHKAVGQPADRPRE 371
            PTHEVLVTGTGGIQW P++ +    E   G+S  NP  S  GKK KA KA     + P+E
Sbjct: 311  PTHEVLVTGTGGIQWHPLQTQ----ESERGNSRGNPHGSRSGKKPKAPKAGEHLTESPQE 366

Query: 372  PLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLVDGYFRLTADSS 431
            P W YFCDF+DI+HVVLKE  V IH QDNKCL L L S+A ALSFV+LVDGYFRLTADSS
Sbjct: 367  PPWTYFCDFQDISHVVLKERRVHIHLQDNKCLLLCLCSQAEALSFVALVDGYFRLTADSS 426

Query: 432  HYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHPYRLILTVAQRS 491
            HYLCHEVAPPRLV SI++GIHGPL++PFVQAKL PEDGLYLI WSTSH +RLILTVA R+
Sbjct: 427  HYLCHEVAPPRLVTSIQNGIHGPLMDPFVQAKLWPEDGLYLIQWSTSHLHRLILTVAHRN 486

Query: 492  QA-PDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRAGDDCFSLRRC 550
             A  +G + LRLRKFPI QQ GAFVL+GWGRSF S+ +L  ALQGC LRAGDDCF L  C
Sbjct: 487  PAXSNGPRGLRLRKFPITQQPGAFVLDGWGRSFASLGDLRLALQGCSLRAGDDCFPLHXC 546

Query: 551  CLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTRTNVYEGRLRV 610
            CLP+P E SNL+IMRG+RA  R LNLSQLSFHRV Q EITQLSHLGQGTRTNVYEG LRV
Sbjct: 547  CLPRPREISNLVIMRGSRAHTRPLNLSQLSFHRVHQDEITQLSHLGQGTRTNVYEGLLRV 606

Query: 611  EGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETASLMSQVSHTHL 670
               G P+EGK+D+  P  PG   GQ+LRVVLKVLDPSHHDIALAFYE ASLMSQVSH HL
Sbjct: 607  ---GGPDEGKVDNGCPPEPGGTSGQQLRVVLKVLDPSHHDIALAFYEXASLMSQVSHMHL 663
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Query: 671  AFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLASALSYLENKNL 730
            AF+HGVCVRG ENI+VTE+VEHGPLDVWLRR+RG VPM WKMVVAQQLASALSYLE+KNL
Sbjct: 664  AFLHGVCVRGSENIIVTEFVEHGPLDVWLRRQRGQVPMTWKMVVAQQLASALSYLEDKNL 723

Query: 731  VHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLAPECLPGGANS 790
            VHGNVCGRNILLARLGL EGT+PFIKLSDPGVG GALSREERVERIPW APECL GG +S
Sbjct: 724  VHGNVCGRNILLARLGLEEGTNPFIKLSDPGVGQGALSREERVERIPWTAPECLSGGTSS 783

Query: 791  LSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCPQLATLTSQCLT 850
            L TA D WGFGATLLEICFDGEAPLQ R PSEKE FY ++H+LPEPSCP+LATLT QCLT
Sbjct: 784  LGTATDMWGFGATLLEICFDGEAPLQGRGPSEKERFYTKKHQLPEPSCPELATLTRQCLT 843

Query: 851  YEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKKIRDLGEGHFGK 910
            YEP QRPSFRTILRDLTRLQP NL     VN DSPASDPTVFHKRYLKKIRDLGEGHFGK
Sbjct: 844  YEPAQRPSFRTILRDLTRLQPQNLVGTSAVNSDSPASDPTVFHKRYLKKIRDLGEGHFGK 903

Query: 911  VSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHIIKYKGCCEDQG 970
            VSLYCYDPTNDGTGEMVAVKALK  CGPQ RSGW++EI+ILRTLYHEHI+KYKGCCEDQG
Sbjct: 904  VSLYCYDPTNDGTGEMVAVKALKEGCGPQLRSGWQREIEILRTLYHEHIVKYKGCCEDQG 963

Query: 971  EKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHYIHRDLAARNVL 1030
            EKS+QLVMEYVPLGSLRDYLPRH +GLAQLLLFAQQICEGMAYLHAQHYIHRDLAARNVL
Sbjct: 964  EKSVQLVMEYVPLGSLRDYLPRHCVGLAQLLLFAQQICEGMAYLHAQHYIHRDLAARNVL 1023

Query: 1031 LDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFYYASDVWSFGVT 1090
            LDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKE KFYYASDVWSFGVT
Sbjct: 1024 LDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKECKFYYASDVWSFGVT 1083

Query: 1091 LYELLTHCDSSQSPPTKFLELIGIAQGQMTVXXXXXXXXXXXXXPRPDKCPCEVYHLMKN 1150
            LYELLT+CDS+QSP TKF ELIG  QGQMTV             PRPD+CPCE+YHLMKN
Sbjct: 1084 LYELLTYCDSNQSPHTKFTELIGHTQGQMTVLRLTELLERGERLPRPDRCPCEIYHLMKN 1143

Query: 1151 CWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC 1187
            CWETEASFRPTF+NL+PIL+T  EKYQGQ PSVFSVC
Sbjct: 1144 CWETEASFRPTFQNLVPILQTAQEKYQGQVPSVFSVC 1180
```

tr Q52KQ2 Q52KQ2_MOUSE **Tyrosine kinase 2 [Tyk2] [Mus musculus (Mouse)]** 1180 AA align

```
 Score = 1871 bits (4846), Expect = 0.0
 Identities = 914/1177 (77%), Positives = 998/1177 (84%), Gaps = 10/1177 (0%)

Query: 12   SKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHIAHKVGITPPCF 71
            SK  G  AQP+   G L VLLHW GP GGEPWVTFS++SLTAEEVCIHIAHKVGITPPC
Sbjct: 13   SKADGTEAQPLVPTGCLMVLLHWPGPEGGEPWVTFSQTSLTAEEVCIHIAHKVGITPPCL 72

Query: 72   NLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREPAVYRCGPPGTE 131
            NLFAL++AQA+VWLPPNHIL+  +D +L  YFR+RFYFRNWHGMNP+EPAVYRCG PG E
Sbjct: 73   NLFALYNAQAKVWLPPNHILDTSQDMNL--YFRMRFYFRNWHGMNPQEPAVYRCGFPGAE 130

Query: 132  ASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFKNESLGMAFLHL 191
             SSD+  QG+QLLD ASFEYLFEQGKHEF+NDV SL +LS+EEEIHHFKNESLGMAFLHL
Sbjct: 131  TSSDRAEQGVQLLDSASFEYLFEQGKHEFMNDVVSLRDLSSEEEIHHFKNESLGMAFLHL 190
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Query: 192  CHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTXXXXXXXXXXXXXXXQPGRLS 251
            CHLAL  G+PLEE+A++ SFK+CIP SFR+HIRQH+ LT               +PG LS
Sbjct: 191  CHLALSRGVPLEEMAREISFKNCIPHSFRQHIRQHNVLTRLRLHRVFRRFLRAFRPGHLS 250

Query: 252  QQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAPTDPGPESAAGP 311
            QQ+VMVKYLATLERLAPRFG+ER+PVCHL +LAQ E +PCYI++SG    DPGPE  +GP
Sbjct: 251  QQVVMVKYLATLERLAPRFGSERIPVCHLEVLAQPERDPCYIQNSGQTAGDPGPELPSGP 310

Query: 312  PTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHKAVGQPADRPRE 371
            PTHEVLVTGTGGIQW P++ +    E   G+S  NP  S  GKK KA KA     + P+E
Sbjct: 311  PTHEVLVTGTGGIQWHPLQTQ----ESERGNSRGNPHGSRSGKKPKAPKAGEHLTESPQE 366

Query: 372  PLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLVDGYFRLTADSS 431
            P W YFCDF+DI+HVVLKE  V IH QDNKCL L L S+A ALSFV+LVDGYFRLTADSS
Sbjct: 367  PPWTYFCDFQDISHVVLKERRVHIHLQDNKCLLLCLCSQAEALSFVALVDGYFRLTADSS 426

Query: 432  HYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHPYRLILTVAQRS 491
            HYLCHEVAPPRLV SI++GIHGPL++PFVQAKL PEDGLYLI WSTSH +RLILTVA R+
Sbjct: 427  HYLCHEVAPPRLVTSIQNGIHGPLMDPFVQAKLWPEDGLYLIQWSTSHLHRLILTVAHRN 486

Query: 492  QA-PDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRAGDDCFSLRRC 550
             A  +G + LRLRKFPI QQ GAFVL+GWGRSF S+ +L  ALQGC LRAGDDCF L  C
Sbjct: 487  PAFSNGPRGLRLRKFPITQQPGAFVLDGWGRSFASLGDLRLALQGCSLRAGDDCFPLHHC 546

Query: 551  CLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTRTNVYEGRLRV 610
            CLP+P E SNL+IMRG+RA  R LNLSQLSFHRV Q EITQLSHLGQGTRTNVYEG LRV
Sbjct: 547  CLPRPREISNLVIMRGSRAHTRPLNLSQLSFHRVHQDEITQLSHLGQGTRTNVYEGLLRV 606

Query: 611  EGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETASLMSQVSHTHL 670
               G P+EGK+D+  P  PG   GQ+LRVVLKVLDPSHHDIALAFYETASLMSQVSH HL
Sbjct: 607  ---GGPDEGKVDNGCPPEPGGTSGQQLRVVLKVLDPSHHDIALAFYETASLMSQVSHMHL 663

Query: 671  AFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLASALSYLENKNL 730
            AF+HGVCVRG ENI+VTE+VEHGPLDVWLRR+RG VPM WKMVVAQQLASALSYLE+KNL
Sbjct: 664  AFLHGVCVRGSENIIVTEFVEHGPLDVWLRRQRGQVPMTWKMVVAQQLASALSYLEDKNL 723

Query: 731  VHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLAPECLPGGANS 790
            VHGNVCGRNILLARLGL EGT+PFIKLSDPGVG GALSREERVERIPW APECL GG +S
Sbjct: 724  VHGNVCGRNILLARLGLEEGTNPFIKLSDPGVGQGALSREERVERIPWTAPECLSGGTSS 783

Query: 791  LSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCPQLATLTSQCLT 850
            L TA D WGFGATLLEICFDGEAPLQ R PSEKE FY ++H+LPEPS P+LATLT QCLT
Sbjct: 784  LGTATDMWGFGATLLEICFDGEAPLQGRGPSEKERFYTKKHQLPEPSSPELATLTRQCLT 843

Query: 851  YEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKKIRDLGEGHFGK 910
            YEP QRPSFRTILRDLTRLQP NL     VN DSPASDPTVFHKRYLKKIRDLGEGHFGK
Sbjct: 844  YEPAQRPSFRTILRDLTRLQPQNLVGTSAVNSDSPASDPTVFHKRYLKKIRDLGEGHFGK 903

Query: 911  VSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHIIKYKGCCEDQG 970
            VSLYCYDPTNDGTGEMVAVKALK  CGPQ RSGW++EI+ILRTLYHEHI+KYKGCCEDQG
Sbjct: 904  VSLYCYDPTNDGTGEMVAVKALKEGCGPQLRSGWQREIEILRTLYHEHIVKYKGCCEDQG 963

Query: 971  EKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHYIHRDLAARNVL 1030
            EKS+QLVMEYVPLGSLRDYLPRH +GLAQLLLFAQQICEGMAYLHAQHYIHRDLAARNVL
Sbjct: 964  EKSVQLVMEYVPLGSLRDYLPRHCVGLAQLLLFAQQICEGMAYLHAQHYIHRDLAARNVL 1023

Query: 1031 LDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFYYASDVWSFGVT 1090
            LDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKE KFYYASDVWSFGVT
```

```
Sbjct: 1024 LDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKECKFYYASDVWSFGVT 1083

Query: 1091 LYELLTHCDSSQSPPTKFLELIGIAQGQMTVXXXXXXXXXXXXXPRPDKCPCEVYHLMKN 1150
          LYELLT+CDS+QSP  KF ELIG  QGQMTV              PRPD+CPCE+YHLMKN
Sbjct: 1084 LYELLTYCDSNQSPHMKFTELIGHTQGQMTVLRLTELLERGERLPRPDRCPCEIYHLMKN 1143

Query: 1151 CWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC 1187
          CWETEASFRPTF+NL+PIL+T  EKYQGQ PSVFSVC
Sbjct: 1144 CWETEASFRPTFQNLVPILQTAQEKYQGQVPSVFSVC 1180
```

tr Q53HA9 Q53HA9_HUMAN **Tyrosine kinase 2 variant (Fragment) [Homo sapiens (Human)]** 822 AA align

```
 Score = 1655 bits (4287), Expect = 0.0
 Identities = 805/822 (97%), Positives = 806/822 (97%)

Query: 1   MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHI 60
           MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHI
Sbjct: 1   MPLRHWGMARGSKPVGDGAQPMAAMGGLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHI 60

Query: 61  AHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREP 120
           AHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREP
Sbjct: 61  AHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYFRIRFYFRNWHGMNPREP 120

Query: 121 AVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFK 180
           AVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFK
Sbjct: 121 AVYRCGPPGTEASSDQTAQGMQLLDPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFK 180

Query: 181 NESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTXXXXXXXXXX 240
           NESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALT
Sbjct: 181 NESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRRHIRQHSALTRLRLRNVFRR 240

Query: 241 XXXXXQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAP 300
                QPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRD GVAP
Sbjct: 241 FLRDFQPGRLSQQMVMVKYLATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDRGVAP 300

Query: 301 TDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHK 360
           TDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHK
Sbjct: 301 TDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHK 360

Query: 361 AVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLV 420
           AVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLV
Sbjct: 361 AVGQPADRPREPLWAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLV 420

Query: 421 DGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHP 480
           DGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHP
Sbjct: 421 DGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLRPEDGLYLIHWSTSHP 480

Query: 481 YRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRA 540
           YRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRA
Sbjct: 481 YRLILTVAQRSQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRA 540

Query: 541 GDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTR 600
           GDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTR
```

```
Sbjct: 541 GDDCFSLRRCCLPQPGETSNLIIMRGARASPRTLNLSQLSFHRVDQKEITQLSHLGQGTR 600

Query: 601 TNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETAS 660
           TNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVL+PSHHDIALAFYETAS
Sbjct: 601 TNVYEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLNPSHHDIALAFYETAS 660

Query: 661 LMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLAS 720
           LMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLAS
Sbjct: 661 LMSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLAS 720

Query: 721 ALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLA 780
           ALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLA
Sbjct: 721 ALSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLA 780

Query: 781 PECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSE 822
           PECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSE
Sbjct: 781 PECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSE 822


 Score = 59.3 bits (142), Expect = 6e-07
 Identities = 54/223 (24%), Positives = 94/223 (41%), Gaps = 26/223 (11%)

Query: 896  YLKKIRDLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKADCGPQHRS---GWKQEIDILR 952
             Y  ++R  G G   +  +   DP   G      ++ +     P H      + +   ++
Sbjct: 604  YEGRLRVEGSGDPEEGKMDDEDPLVPGRDRGQELRVVLKVLNPSHHDIALAFYETASLMS 663

Query: 953  TLYHEHIIKYKGCCEDQGEKSLQLVMEYVPLGSLRDYLPRHS--IGLAQLLLFAQQICEG 1010
              + H H+    G C  +G +++ +V EYV  G L  +L R    + +A  ++ AQQ+
Sbjct: 664  QVSHTHLAFVHGVCV-RGPENI-MVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLASA 721

Query: 1011 MAYLHAQHYIHRDLAARNVLL-------DNDRLVKIGDFGLAKAVPEGHEYYRVREDGDS 1063
           ++YL  ++ +H ++  RN+LL             +K+ D G+              RE+
Sbjct: 722  LSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALS-------REERVE 774

Query: 1064 PVFWYAPECLK--EYKFYYASDVWSFGVTLYELLTHCDSSQSP 1104
              + W APECL         A D W FG TL E+   C   ++P
Sbjct: 775  RIPWLAPECLPGGANSLSTAMDKWGFGATLLEI---CFDGEAP 814
```

tr Q6GPK5_XENLA **MGC83617 protein [MGC83617] [Xenopus laevis (African clawed frog)]** 1179 AA align

```
 Score = 1345 bits (3482), Expect = 0.0
 Identities = 688/1186 (58%), Positives = 852/1186 (71%), Gaps = 55/1186 (4%)

Query: 27   GLKVLLHWAGPGGGEPWVTFSESSLTAEEVCIHIAHKVGITPPCFNLFALFDAQAQVWLP 86
           GL+V L+W+   G E +VT+S+  +TAE+VCIHI+ ++GITP C+ LEAL+D   + W P
Sbjct: 24   GLRVFLYWSN--GKEHYVTYSQGQITAEDVCIHISERLGITPLCYTLFALYDVHGKYWYP 81

Query: 87   PNHILEIPRDASLMLYFRIRFYFRNWHGMNPREPAVYRCGPPGTEASSDQTA--QGMQLL 144
           P+H+  I +D  L L+FR+R+YFRNWHGMN +EP V+R  P   + S +++   Q   +L
Sbjct: 82   PDHVFTITKDMKLFLHFRMRYYFRNWHGMNEKEPVVFRNVPKSRDGSEERSRIEQAGAIL 141

Query: 145  DPASFEYLFEQGKHEFVNDVASLWELSTEEEIHHFKNESLGMAFLHLCHLALRHGIPLEE 204
           D ASFEYLFEQGK +FVNDV SL +   E++IH FKNESLGMA LHL H+A++  + LEE
```

```
Sbjct: 142  DLASFEYLFEQGKFDFVNDVVSLKDFPMEQDIHRFKNESLGMAVLHLSHIAIKKKVSLEE 201

Query: 205  VAKKTSFKDCIPRSFRRHIRQHSALTXXXXXXXXXXXXX-----XXQPGRLSQQMVMVKY 259
            VAK+ SFK+CIP+SF R I+Q++ LT                    PG+L+++ +M KY
Sbjct: 202  VAKQISFKECIPKSFCRQIQQNNYLTKFRMKNVFKKFVRRFHLHTVSPGKLTEEDIMYKY 261

Query: 260  LATLERLAPRFGTERVPVCHLRLLAQAEGEPCYIRDSGVAPTDPGPESAAGPPTHEVLVT 319
            L+TLE LA RFG E      L L A+ E  P Y+    +  T+          TH+V+V+
Sbjct: 262  LSTLENLATRFGCEVFKALSLELPAEGEKLPFYLNGGYMEHTETVNREPIS--THQVMVS 319

Query: 320  GTGGIQWWPVEEEVNKEEGSSGSSGRNPQASLFGKKAKAHKAVGQPADRPR------EPL 373
            G  GIQ+  ++EE   E  +        Q   F KK+      GQ A +P+      EP
Sbjct: 320  GMDGIQYRVIKEEETAEVST--------QRHYFSKKSWVK---GQKASKPQQITEKNEPK 368

Query: 374  WAYFCDFRDITHVVLKEHCVSIHRQDNKCLELSLPSRAAALSFVSLVDGYFRLTADSSHY 433
            W  FCDF+DITH+V+ +  VS+  QDN+CLE++LPS   ALSFVSLVDGYFRLT DS+HY
Sbjct: 369  WVTFCDFQDITHIVISKSRVSVSCQDNRCLEIALPSCEDALSFVSLVDGYFRLTTDSNHY 428

Query: 434  LCHEVAPPRLVMSIRDGIHGPLLEPFVQAKLR---PEDGLYLIHWSTSHPYRLILTVAQR 490
            LCHEVAPPRLVMS+ +GIHGPL E +V  KLR    E+G+Y+I WS      +I+ V
Sbjct: 429  LCHEVAPPRLVMSVANGIHGPLQEQYVVQKLRREEQEEGVYIIRWSAFTFNIIIMAVKST 488

Query: 491  SQAPDGMQSLRLRKFPIEQQDGAFVLEGWGRSFPSVRELGAALQGCLLRAGDDCFSLRRC 550
            SQ+    +    ++F IE++   F LE W R F SV+EL  +L+GC L++G + F+++++C
Sbjct: 489  SQS----KGFAYKQFKIEKKGEVFSLEDWDREFHSVKELVESLRGCTLKSGKETFTVKKC 544

Query: 551  CLPQPGETSNLIIMR-GARASPRT----LNLSQLSFHRVDQKEITQLSHLGQGTRTNVYE 605
             LP+ GE SNL + R G   +  RT    LNLSQLSFH++ + EI Q +HLGQGTRTN+Y+
Sbjct: 545  ILPKSGEVSNLTVSRRGKNSKDRTVSKNLNLSQLSFHQIRKHEILQKAHLGQGTRTNIYD 604

Query: 606  GRLRV-EGS---GDPEEGKMDDEDPLVPGRDRGQELRVVLKVLDPSHHDIALAFYETASL 661
            G L V EGS    D E G++++             +LRVVLKVLDPSH DIALAF+ETASL
Sbjct: 605  GMLLVSEGSEQESDFESGELNNNS---------HDLRVVLKVLDPSHRDIALAFFETASL 655

Query: 662  MSQVSHTHLAFVHGVCVRGPENIMVTEYVEHGPLDVWLRRERGHVPMAWKMVVAQQLASA 721
            MSQVSH HL FVHGVCVR  ENIMV E++EHGPLDV LR+++  +   WK  VA+QLASA
Sbjct: 656  MSQVSHIHLVFVHGVCVRESENIMVEEFIEHGPLDVCLRKDKLRIKTEWKFTVARQLASA 715

Query: 722  LSYLENKNLVHGNVCGRNILLARLGLAEGTSPFIKLSDPGVGLGALSREERVERIPWLAP 781
            LSYLE+KNLVHGNVC +NILLAR GL E +SPFIKLSDPGV    LSREERVERIPW+AP
Sbjct: 716  LSYLEDKNLVHGNVCAKNILLARKGLEENSSPFIKLSDPGVTFTVLSREERVERIPWIAP 775

Query: 782  ECLPGGANSLSTAMDKWGFGATLLEICFDGEAPLQSRSPSEKEHFYQRQHRLPEPSCPQL 841
            EC+    +SLSTA DKW FG TLLEICF+GE PL+ R+P EKE FY+++  LPEPSC +L
Sbjct: 776  ECVRN-ISSLSTAADKWSFGTTLLEICFNGEVPLKERTPPEKERFYEKELGLPEPSCKEL 834

Query: 842  ATLTSQCLTYEPTQRPSFRTILRDLTRLQPHNLADVLTVNPDSPASDPTVFHKRYLKKIR 901
            A L  QC  Y    RPSFRTILR+LT+LQP  L D+  ++P S  +DPTVF KRYLKKIR
Sbjct: 835  ADLIGQCHNYNAEGRPSFRTILRELTQLQPDVLPDIAAISPVS-ITDPTVFQKRYLKKIR 893

Query: 902  DLGEGHFGKVSLYCYDPTNDGTGEMVAVKALKADCGPQHRSGWKQEIDILRTLYHEHIIK 961
            +LGEGHFGKVSLYCYDP NDGTGEMVAVK+LK+ C  Q  S WK EI IL+TLYHE+I+K
Sbjct: 894  ELGEGHFGKVSLYCYDPNNDGTGEMVAVKSLKSGCSQQLESSWKGEIKILKTLYHENIVK 953

Query: 962  YKGCCEDQGEKSLQLVMEYVPLGSLRDYLPRHSIGLAQLLLFAQQICEGMAYLHAQHYIH 1021
            YKGCC +QG+K +QL+MEYVPLGSLRDYLP+H++ LAQ+LLFAQQICEGMAYLH+QHYIH
Sbjct: 954  YKGCCSEQGDKIVQLIMEYVPLGSLRDYLPKHNVSLAQILLFAQQICEGMAYLHSQHYIH 1013
```

```
Query: 1022 RDLAARNVLLDNDRLVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYAPECLKEYKFYYA 1081
            RDLAARNVL++N+ +VKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYA ECLKE KF+YA
Sbjct: 1014 RDLAARNVLVENENVVKIGDFGLAKAVPEGHEYYRVREDGDSPVFWYATECLKECKFFYA 1073

Query: 1082 SDVWSFGVTLYELLTHCDSSQSPPTKFLELIGIAQGQMTVXXXXXXXXXXXXXPRPDKCP 1141
            SDVWSFGVT YELLT CDS  SPP KF+E+IG+ QGQMTV             P P+ CP
Sbjct: 1074 SDVWSFGVTFYELLTRCDSYLSPPAKFIEMIGVTQGQMTVVRLIDLLERGQRLPCPNDCP 1133

Query: 1142 CEVYHLMKNCWETEASFRPTFENLIPILKTVHEKYQGQAPSVFSVC 1187
             E+Y LMKNCWETEA+FRPTF +LIPILK+ R  Y  QAPSVFS+C
Sbjct: 1134 LEIYKLMKNCWETEANFRPTFNHLIPILKSYHNTYSTQAPSVFSLC 1179
```

tr Q9PWM9 **Tyrosine kinase JAK1 [JAK1] [Gallus gallus (Chicken)]** 1150 AA
Q9PWM9_CHICK

align

Score = 984 bits (2544), Expect = 0.0
Identities = 525/1147 (45%), Positives = 717/1147 (61%), Gaps = 60/1147 (5%)

```
Query: 44   VTFSESSLTAEEVCIHIAHKVGITPPCFNLFALFDAQAQVWLPPNHILEIPRDASLMLYF 103
            + ++    T+EE+CI  A K  I+P C NLFALFD   ++W  PN + +I    S  LY+
Sbjct: 48   ICYTSGEFTSEELCIEAAQKCSISPLCHNLFALFDENRRLWYAPNQVFKIDEKTSQRLYY 107

Query: 104  RIRFYFRNWHGMNPREPAVYRCGPPGTEASSDQ--TAQGMQLLDPASFEYLFEQGKHEFV 161
            R+R+YF NWHG +  EP+V+R  P  ++ S D+    +G  +LD  S EY+F QG+++ V
Sbjct: 108  RMRYYFTNWHGTSENEPSVWRHSPKKSKNSYDKKLAPEGTPILDANSLEYIFAQGQYDLV 167

Query: 162  NDVASLWELSTEEEIHHFKNESLGMAFLHLCHLALRHGIPLEEVAKKTSFKDCIPRSFRR 221
             ++A + +   ++E+H  +NE LGMA L + H A++  + L E+ K  S+K  IP +  +
Sbjct: 168  RELAPIRDPKNDQEVHEIENECLGMAVLAISHYAIKKNVKLPELPKDISYKHYIPETLNK 227

Query: 222  HIRQHSALTXXXXXXXXXXXXXXQ-----PGRLSQQMVMVKYLATLERLAPRFGTERVP 276
             IRQ + LT                    +S + + VKYL+T+E L   +G E
Sbjct: 228  TIRQRNFLTRIRINNVFKHFLKEFNNKTICDSSVSPRDLKVKYLSTMETLTKYYGAEIFE 287

Query: 277  VCHLRLLAQAEGEPCYIRDSGVAPTDPGPESAAGPPTHEVLVTGTGGIQWWPVEEEVNKE 336
               L + +++E       D  + P              +EV+VTG  GIQW      V  E
Sbjct: 288  TSSLLISSESEINRFNCGDGEIIPL------------YEVIVTGNNGIQWRLKPSSVQTE 335

Query: 337  EGSSGSSGRNPQASLFGKKAKAHKAVGQPADRPR-EPLWAYFCDFRDITHVVLKEHCVSI 395
                        KK K+   + +  DR +   LW  F  F +ITH+V+KE  VSI
Sbjct: 336  ----------------KKKSDGKIKKDEDRYKTRDLWNNFSYFPEITHIVIKESTVSI 378

Query: 396  HRQDNKCLELSLPSRAAALSFVSLVDGYFRLTADSSHYLCHEVAPPRLVMSIRDGIHGPL 455
            ++QDNK +EL L S   ALSF SL+DGYFRLTAD+ HYLC +VAPP +  +I++G HGP+
Sbjct: 379  NKQDNKKMELKLSSHDEALSFASLIDGYFRLTADAHHYLCTDVAPPLIEHNIKNGCHGPI 438

Query: 456  LEPFVQAKLRPED---GLYLIHWSTSHPYRLILTVAQRSQAPDGMQ-SLRLRKFPIEQQD 511
               +  +LR E     G+Y++ WS ++ + LIL      + P+ +  S++ + F IE +
Sbjct: 439  CTEYAINRLRQEGNEAGMYVLRWSCTN-FNLILMTVTCLEGPEMINNSVQYKNFQIEVKK 497

Query: 512  GAFVLEGWGRSFPSVRELGAALQGCLLRAGDDCFSLRRCCLPQPGETSNLIIM-RGARAS 570
            G + L G  RSF S++EL   L+G +LR  + F+L+RCC P+P E SNL++  + A+
Sbjct: 498  GGYFLHGSNRSFASLKELMDHLKGQILRTDNISFTLKRCCQPKPREISNLLVATKKAQEC 557
```

RasGAP in breast cancer **cells**
AUTHOR: Zrihan-Licht S (Reprint); Fu Y; Settleman J; Schinkmann K; Shaw L; Keydar I; Avraham S; Avraham Hava
AUTHOR ADDRESS: Beth Israel Deaconess Med Ctr, Harvard Med Sch, Boston, MA, USA**USA
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BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: T-47D cell line (Hominidae)--human breast cancer cell line
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: p-190 RhoGAP protein--RAFTK-PYK-2 tyrosine kinase mediation, RasGAP protein association, tumor cell expression
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
02508 Cytology - Human
24004 Neoplasms - Pathology, clinical aspects and systemic effects
00520 General biology - Symposia, transactions and proceedings
BIOSYSTEMATIC CODES:
86215 Hominidae

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11763494 Genuine Article#: 600ZN Number of References: 0
Title: The focal adhesion kinase (FAK) family member PYK2 **is central for** inflammatory **crystal-induced chondrocyte activation.**
Author(s): Liote F; Rose D; Terkeltaub R; Metz D; Liu-Bryan R
Corporate Source: VAMC,San Diego//CA/; Univ Calif San Diego,San Diego//CA/92103; Hop Lariboisiere,INSERM U349, Ctr Viggo Petersen,F-75475 Paris//France/
Journal: ARTHRITIS AND RHEUMATISM, 2002, V46, N9,S (SEP), PS592-S592
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Journal Subject Category: RHEUMATOLOGY

11/9/12 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11089258 EMBASE No: 2001106893
RAFTK/ Pyk2 **-mediated signaling in breast** cancer **cells**

11/9/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15096432 PMID: 14654952

Coupling of RAFTK/ Pyk2 **kinase with c-Abl and their role in the migration of breast** cancer **cells.**

Zrihan-Licht Sheila; Avraham Shalom; Jiang Shuxian; Fu Yigong; Avraham Hava Karsenty

Division of Experimental Medicine, Beth Israel Deaconess Medical Center, Harvard Institutes of Medicine, Boston, MA 02115, USA.

International journal of oncology (Greece) Jan 2004, 24 (1) p153-9, ISSN 1019-6439 Journal Code: 9306042

Contract/Grant No.: 1R01CA096805; CA; NCI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Mitogen-induced changes in the actin cytoskeleton are accompanied by changes in the tyrosine phosphorylation of several proteins in focal adhesions. In this study, we have investigated the role of RAFTK (also termed Pyk2/CAK-beta), a cytoplasmic tyrosine kinase related to focal adhesion kinase (FAK), in heregulin-mediated signal transduction in breast cancer cells. Stimulation of T47D cells with heregulin (HRG) induced the tyrosine phosphorylation of RAFTK and the formation of a multiprotein complex. Maximal phosphorylation of the proteins participating in this complex occurred within 2 h of HRG stimulation. Analyses of the members of the HRG-stimulated complex revealed that RAFTK associated with p190 RhoGAP (p190), RasGAP, c-Abl as well as with the focal adhesion molecules p130cas and paxillin. c-Abl was found to be associated with RAFTK through the region of RAFTK containing amino acids 419-1009. Site-directed mutagenesis of Y881 aa within the RAFTK sequence abolished the binding of RAFTK to c-Abl, indicating that the tyrosine residue 881 of RAFTK is the c-Abl binding site within the RAFTK molecule. Overexpression of wild-type RAFTK significantly enhanced breast cancer cell invasion, while overexpression of the mutants Tyr402 or Tyr881 of RAFTK inhibited this migration. Therefore, RAFTK serves as a mediator and an integration point between focal adhesion molecules in HRG-mediated signaling in T47D breast cancer cells.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Cell Movement--physiology--PH; *Protein-Tyrosine Kinase --metabolism--ME; *Proto-Oncogene Proteins c-abl--metabolism--ME; Breast Neoplasms--genetics--GE; Breast Neoplasms--metabolism--ME; Breast Neoplasms--pathology--PA; Cell Adhesion Molecules--metabolism--ME; Cell Line; Cell Line, Tumor; Cell Movement--drug effects--DE; Cell Movement --genetics--GE; Cytoskeletal Proteins--metabolism--ME; Electrophoresis, Polyacrylamide Gel; Guanine Nucleotide Exchange Factors--metabolism--ME; Humans; Mutation; Neuregulin-1--pharmacology--PD; Nuclear Proteins --metabolism--ME; Phosphoproteins--metabolism--ME; Phosphorylation --drug effects--DE; Protein Binding; Protein-Tyrosine Kinase--genetics--GE; Proteins--metabolism--ME; Proto-Oncogene Proteins c-abl--genetics--GE; Tyrosine--metabolism--ME

CAS Registry No.: 0 (Cell Adhesion Molecules); 0 (Cytoskeletal Proteins); 0 (GAP-associated protein p190); 0 (Guanine Nucleotide Exchange Factors); 0 (Neuregulin-1); 0 (Nuclear Proteins); 0 (Phosphoproteins); 0 (Proteins); 0 (RBL2 protein, human); 0

(paxillin); 55520-40-6 (Tyrosine)
Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.112 (Proto-Oncogene Proteins c-abl)
Record Date Created: 20031205
Record Date Completed: 20040817

11/9/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14256734 PMID: 12063569
Csk homologous kinase associates with RAFTK/ Pyk2 **in breast** cancer **cells and negatively regulates its activation and breast** cancer **cell migration.**
McShan Gina D; Zagozdzon Radoslaw; Park Shin-Young; Zrihan-Licht Sheila; Fu Yigong; Avraham Shalom; Avraham Hava
Division of Experimental Medicine, Beth Israel Deaconess Medical Center, Harvard Institutes of Medicine, Boston, MA 02115, USA.
International journal of oncology (Greece) Jul 2002, 21 (1) p197-205 , ISSN 1019-6439 Journal Code: 9306042
Contract/Grant No.: CA76226; CA; NCI; CA76772; CA; NCI; HL51456; HL; NHLBI; HL55445; HL; NHLBI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Our recent observations indicated that RAFTK (also termed Pyk2 and CAK-beta) participated in intracellular signaling upon heregulin (HRG) stimulation and promoted breast carcinoma invasion. Furthermore, studies from our group indicate that the Csk homologous kinase (CHK), a member of the Csk family, directly associates with HER2/Neu and down-regulates HER2/Neu-mediated Src kinase activation in breast cancer cells upon heregulin stimulation. Since activation of RAFTK is associated with the activity of Src family kinases, we analyzed whether CHK is capable of opposing HRG-induced activation of RAFTK. Stimulation of human T47D breast cancer cells with HRG induced the tyrosine phosphorylation of RAFTK and its association with CHK in vitro and in vivo. This interaction was mediated through the Src binding site (amino acid residue at 402) of RAFTK and the SH2 domain of CHK. RAFTK phosphorylation downstream of the activated HER2/Neu was greatly reduced in the presence of CHK. Maximal inhibition of RAFTK phosphorylation by CHK required the kinase activity of CHK. Furthermore, CHK inhibited the tyrosine phosphorylation of the focal adhesion-associated protein, paxillin, and inhibited HRG-induced T47D breast cancer cell migration. These findings indicate the role of CHK as a negative regulator in HRG- and RAFTK-mediated intracellular signaling in breast cancer cells.
Tags: Female; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.
Descriptors: *Breast Neoplasms--pathology--PA; *Neuregulin-1 --pharmacology--PD; *Protein-Tyrosine Kinase--metabolism--ME; *Proto-Oncogene Protein pp60(c-src); Blotting, Western; Breast Neoplasms--metabolism--ME ; Cell Movement--drug effects--DE; Cytoskeletal Proteins--metabolism--ME; Down-Regulation--physiology--PH; Focal Adhesions; Humans; Megakaryocytes; Neoplasm Invasiveness; Phosphoproteins--metabolism--ME; Phosphorylation; Plasmids; Precipitin Tests; Protein Binding; Receptor, erbB-2--metabolism --ME; Recombinant Proteins--metabolism--ME; Signal Transduction;

12784810 PMID: 10713673

RAFTK/ Pyk2 **tyrosine kinase mediates the association of p190 RhoGAP with RasGAP and is involved in breast** cancer **cell invasion.**

Zrihan-Licht S; Fu Y; Settleman J; Schinkmann K; Shaw L; Keydar I; Avraham S; Avraham H

Division of Experimental Medicine, Beth Israel Deaconess Medical Center, Harvard Institutes of Medicine, 4 Blackfan Circle, Boston, Massachusetts, MA 02115, USA.

Oncogene (ENGLAND) Mar 2 2000, 19 (10) p1318-28, ISSN 0950-9232 Journal Code: 8711562

Contract/Grant No.: CA76226; CA; NCI; HL51456; HL; NHLBI; HL55455; HL; NHLBI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Focal adhesions and actin cytoskeleton are involved in cell growth, shape and movement and in tumor invasion. Mitogen-induced changes in actin cytoskeleton are accompanied by changes in the tyrosine phosphorylation of several focal adhesion proteins. In this study, we have investigated the role of RAFTK, a cytoplasmic tyrosine kinase related to focal adhesion kinase (FAK), in heregulin-mediated signal transduction in breast cancer cells. Stimulation of T47D cells with heregulin (HRG) induced the tyrosine phosphorylation of RAFTK and the formation of a multiprotein complex. Analyses of the members of the HRG-stimulated complex revealed that RAFTK is associated with p190 RhoGAP (p190), RasGAP and ErbB-2, and plays an essential role in mediating the tyrosine phosphorylation of p190 by Src. Mutation of the Src binding site within RAFTK (402) abolished the phosphorylation of p190. In addition, upon HRG stimulation of T47D cells, association of ErbB-2 with RAFTK was observed and found to be indirect and mediated by Src. Expression of wild-type RAFTK (WT) significantly increased MDA-MB-435 and MCF-7 breast cancer cell invasion, while expression of the kinase-mutated RAFTK-R457 (KM) or the Src binding site mutant RAFTK (402) did not affect this cell invasion. Furthermore, HRG leads to the activation of MAP kinase which is mediated by RAFTK. These findings indicate that RAFTK serves as a mediator and an integration point between the GAP proteins and HRG-mediated signaling in breast cancer cells, and implicate RAFTK involvement in the MAP kinase pathway and in breast cancer cell invasion.

Tags: Female; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Breast Neoplasms--pathology--PA; *Guanine Nucleotide Exchange Factors; *Nuclear Proteins--metabolism--ME; *Phosphoproteins --metabolism--ME; *Protein-Tyrosine Kinase--metabolism--ME; *ras GTPase-Activating Proteins--metabolism--ME; Breast Neoplasms--metabolism --ME; Humans; Mitogen-Activated Protein Kinases--metabolism--ME; Neoplasm Invasiveness; Neuregulin-1--pharmacology--PD; Phosphorylation; Protein Binding; Proto-Oncogene Protein pp60(c-src)--metabolism--ME; Receptor, erbB-2--metabolism--ME; Tyrosine

CAS Registry No.: 0 (GAP-associated protein p190); 0 (Guanine Nucleotide Exchange Factors); 0 (Neuregulin-1); 0 (Nuclear Proteins); 0 (Phosphoproteins); 0 (ras GTPase-Activating Proteins); 55520-40-6 (Tyrosine)

Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112

S10 43 S8
S11 16 RD (unique items)
? s s4 and arthrit?/ti
176858 S4
264060 ARTHRIT?/TI
S12 182 S4 AND ARTHRIT?/TI
? s s4 and colitis?/ti
176858 S4
82418 COLITIS?/TI
S13 28 S4 AND COLITIS?/TI
? s s4 and crohn?/ti
176858 S4
59411 CROHN?/TI
S14 25 S4 AND CROHN?/TI
? t s13/6/all

13/6/1 (Item 1 from file: 73)
13229367 EMBASE No: 2005293388
Diminished cytokine signalling against bacterial components in mononuclear leucocytes from ulcerative colitis **patients after leukocytapheresis**
2005

13/6/2 (Item 2 from file: 73)
13185295 EMBASE No: 2005250837
Mutations of the BRAF gene in ulcerative colitis **-related colorectal carcinoma**
10 JUL 2005

13/6/3 (Item 3 from file: 73)
13155092 EMBASE No: 2005219832
Amelioration of experimental colitis **by Na-H exchanger-1 inhibitor amiloride is associated with reversal of IL-1beta and ERK mitogen-activated protein kinase**
2005

13/6/4 (Item 4 from file: 73)
13128173 EMBASE No: 2005188840
Therapeutic effect of adenoviral-mediated hepatocyte growth factor gene administration on TNBS-induced colitis **in mice**
22 APR 2005

13/6/5 (Item 5 from file: 73)
13074848 EMBASE No: 2005135175
Activation of nuclear factor kappaB in colonic mucosa from patients with collagenous and ulcerative colitis
2005

13/6/6 (Item 6 from file: 73)
12968374 EMBASE No: 2005028876
Selective loss of NGF-sensitive neurons following experimental colitis
2005

13/6/7 (Item 7 from file: 73)
12930832 EMBASE No: 2004521125
Activator protein-1 signalling pathway and apoptosis are modulated by poly(ADP-ribose) polymerase-1 in experimental colitis
2004

13/6/8 (Item 8 from file: 73)
12818303 EMBASE No: 2004412304
Two TTX-resistant NaSUP+ currents in mouse colonic dorsal root ganglia neurons and their role in colitis -induced hyperexcitability
2004

13/6/9 (Item 9 from file: 73)
12815551 EMBASE No: 2004409328
Catalposide, a compound isolated from Catalpa ovata, attenuates induction of intestinal epithelial proinflammatory gene expression and reduces the severity of trinitrobenzene sulfonic acid-induced colitis in mice
2004

13/6/10 (Item 10 from file: 73)
12783534 EMBASE No: 2004377264
Sudden onset of colitis after ablation of secretin-expressing lymphocytes in transgenic mice
2004

13/6/11 (Item 11 from file: 73)
12745246 EMBASE No: 2004343187
IKKbeta links inflammation and tumorigenesis in a mouse model of colitis -associated cancer
06 AUG 2004

13/6/12 (Item 12 from file: 73)
12364569 EMBASE No: 2003483633
Investigation and management of ischemic colitis
2003

13/6/13 (Item 13 from file: 73)
12078572 EMBASE No: 2003181225
Rho kinase blockade prevents inflammation via nuclear factor kappaB inhibition: Evidence in Crohn's disease and experimental colitis
01 MAY 2003

13/6/14 (Item 14 from file: 73)
11941215 EMBASE No: 2003050094
The more an ulcerative colitis is repeated, the more the risk of colorectal carcinogenesis is increased in mice
2002

13/6/15 **(Item 15 from file: 73)**
11695727 EMBASE No: 2002253297
Hepatitis C, collagenous colitis **, dermatomyositis occurring in the same patient [8]**
2002

13/6/16 **(Item 16 from file: 73)**
11652423 EMBASE No: 2002223886
NaSUP+/HSUP+ exchanger blockade inhibits enterocyte inflammatory response and protects against colitis
2002

13/6/17 **(Item 17 from file: 73)**
11643296 EMBASE No: 2002214838
Dichotomal role of inhibition of p38 MAPK with SB 203580 in experimental colitis
2002

13/6/18 **(Item 18 from file: 73)**
11624652 EMBASE No: 2002196463
Protective effects of neurokinin-1 receptor during colitis **in mice: Role of the epidermal growth factor receptor**
2002

13/6/19 **(Item 19 from file: 73)**
11156425 EMBASE No: 2001172757
Impaired sensitivity to betaSUB2 integrin-blocking in ICAM-1-mediated neutrophil migration in ulcerative colitis
2001

13/6/20 **(Item 20 from file: 73)**
11057941 EMBASE No: 2001060272
Polysaccharides extracted from human tubercle bacilli (specific substance of Maruyama) reduces carcinogenesis in murine ulcerative colitis
2000

13/6/21 **(Item 21 from file: 73)**
10966077 EMBASE No: 2001010685
Adenosine kinase inhibitor GP515 improves experimental colitis **in mice**
2001

13/6/22 **(Item 22 from file: 73)**
10584718 EMBASE No: 2000049938
Alterations in protein kinase C isoforms in experimentally-induced colitis **in the rat**
2000

13/6/23 **(Item 23 from file: 73)**
07647920 EMBASE No: 1999121313

Protein kinase C mediates experimental colitis **in the rat**
1999

13/6/24 **(Item 24 from file: 73)**
06909830 EMBASE No: 1997194272
Fever, acute colitis **and kidney failure in a 44-year-old woman**
FIEVRE, COLITE AIGUE ET INSUFFISANCE RENALE CHEZ UNE FEMME DE 44 ANS
1997

13/6/25 **(Item 25 from file: 73)**
06837296 EMBASE No: 1997119806
Differential activation of total and EGF receptor (EGF-R) tyrosine kinase (tyr-k) in the rectal mucosa in patients with adenomatous polyps, ulcerative colitis **and colon cancer**
1997

13/6/26 **(Item 26 from file: 73)**
05666942 EMBASE No: 1994074031
Elevated c-Src tyrosine kinase activity in premalignant epithelia of ulcerative colitis
1994

13/6/27 **(Item 27 from file: 73)**
05099257 EMBASE No: 1992239473
Increased protein tyrosine kinase activity of the colonic mucosa in ulcerative colitis
1992

13/6/28 **(Item 28 from file: 73)**
04994698 EMBASE No: 1992134914
Protein kinase C activity of colonic mucosa in ulcerative colitis
1992
? ds

Set	Items	Description
S1	3335	E3-E50
S2	86	'FOCAL ADHESION KINASE 2'
S3	173883	'FOCAL ADHESION KINASE 2' OR DC='D4.680.265.60.680' OR R4:-R10
S4	176858	S1 OR S2 OR S3
S5	90232	S4 AND (INCREASE? OR DECREASE? OR REDUC? OR HIGHER? OR LOWER? OR INSUFFIC? OR DEPLET? OR DEFICIENT?)
S6	32420	S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)
S7	4690	S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)/TI
S8	43	S4/TI (100N) (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)
S9	2437	S4 AND ((CONNECTIVE? (3N) TISSUE?) OR ARTHRIT? OR DEGENERATIV?)
S10	43	S8
S11	16	RD (unique items)
S12	182	S4 AND ARTHRIT?/TI

S13 28 S4 AND COLITIS?/TI
S14 25 S4 AND CROHN?/TI
? t s14/6,kwic/all
>>>KWIC option is not available in file(s): 399

14/6,KWIC/1 (Item 1 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

13194882 EMBASE No: 2005241589
Nod2 and Crohn **'s disease: Many connected highways**
21 MAY 2005

Nod2 and Crohn **'s disease: Many connected highways**
EMTREE CODES:
...G3.880.750; D24.35.150.150; D24.35.190.150; D4.680.190.150;
D4.680.265.60.680 ; G3.560.710.730; D4.680; D4.140.345; D4.680...

14/6,KWIC/2 (Item 2 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

13145547 EMBASE No: 2005187520
Inhibition of RICK/nuclear factor-kappaB and p38 signaling attenuates the inflammatory response in a murine model of Crohn **disease**
15 APR 2005

...nuclear factor-kappaB and p38 signaling attenuates the inflammatory response in a murine model of Crohn **disease**
EMTREE CODES:
...D24.35.880; D4.680.140.625; G3.560.560.460.350.880; D4.270;
D4.680.265.60.680 ; D2.20.50.50.10.680; D2.20.50.50.10...

14/6,KWIC/3 (Item 3 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

13056041 EMBASE No: 2005118186
Antibodies to tumor necrosis factor-alpha in the treatment of Crohn **'s disease**
2005

Antibodies to tumor necrosis factor-alpha in the treatment of Crohn **'s disease**
EMTREE CODES:
...750.190; D24.35.880; D4.680.140.625; G3.560.560.460.350.880;
D4.680.265.60.680 ; D4.140.345; D4.680.350; D24.25.25; D4.680...

14/6,KWIC/4 (Item 4 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

13044519 EMBASE No: 2005099948
Rhabdomyolysis associated with Crohn **'s disease, probably mediated by myositis [4]**
2005

Rhabdomyolysis associated with Crohn **'s disease, probably mediated by myositis [4]**

EMTREE CODES:
...D9.50.80.40; D2.20.50.50.25.880; C6.425.40; D19.10; **D4.680.265.60.680** ; D4.270

14/6,KWIC/5 (Item 5 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

12986051 EMBASE No: 2005045357
Differential modulation of p38 mitogen activated protein kinase and STAT3 signalling pathways by infliximab and etanercept in intestinal T cells from patients with Crohn **'s disease (multiple letter) [9]**
2005

...and STAT3 signalling pathways by infliximab and etanercept in intestinal T cells from patients with Crohn **'s disease (multiple letter) [9]**
EMTREE CODES:
...680.48.560; G2.440.30.560; D9.20; D14.30.40; D4.680.750;
D4.680.265.60.680 ; D4.270; D24.35.880; G3.560.560.460.350.880...

14/6,KWIC/6 (Item 6 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

12919452 EMBASE No: 2004521760
Efficacy and safety of tumor necrosis factor antagonists in Crohn **'s disease: Overview of randomized clinical studies**
2004

Efficacy and safety of tumor necrosis factor antagonists in Crohn **'s disease: Overview of randomized clinical studies**
EMTREE CODES:
...345.440; D4.680.700.440; G2.440.465; D4.680.700; D4.680.345;
D4.680.265.60.680 ; D24.15; D4.65; G2.440.40; D1.20.230

14/6,KWIC/7 (Item 7 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

12782218 EMBASE No: 2004375365
Celastrol inhibits pro-inflammatory cytokine secretion in Crohn **'s disease biopsies**
24 SEP 2004

Celastrol inhibits pro-inflammatory cytokine secretion in Crohn **'s disease biopsies**
EMTREE CODES:
...D24.35.150.150; D24.35.190.150; D4.680.190.150; D4.140.490;
D4.680.265.60.680 ; D1.20.230

14/6,KWIC/8 (Item 8 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

12715120 EMBASE No: 2004315945
Critical involvement of stress-activated mitogen-activated protein

kinases in the regulation of intracellular adhesion molecule-1 in serosal fibroblasts isolated from patients with Crohn 's disease
2004

...in the regulation of intracellular adhesion molecule-1 in serosal fibroblasts isolated from patients with Crohn 's disease
EMTREE CODES:
...20.10; B2.60.60.60.10.40; J2.40.10; J2.10; L1; J1; **D4.680.265.60.680** ;
D24.15.140.490.510; D4.65.140.490.510; G2...

14/6,KWIC/9 (Item 9 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

12315002 EMBASE No: 2003429682
The mitogen-activated protein kinase p38 - A new molecular target for anti-inflammatory therapy in Crohn 's disease?
2003

The mitogen-activated protein kinase p38 - A new molecular target for anti-inflammatory therapy in Crohn 's disease?
EMTREE CODES:
...560.460.350; A13; J2.20.10; B2.60.60.60.10.40; J1.100;
D4.680.265.60.680 ; D23.40.520.560; D24.25.25.560; D4.680.48...

14/6,KWIC/10 (Item 10 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

12078572 EMBASE No: 2003181225
Rho kinase blockade prevents inflammation via nuclear factor kappaB inhibition: Evidence in Crohn 's disease and experimental colitis
01 MAY 2003

Rho kinase blockade prevents inflammation via nuclear factor kappaB inhibition: Evidence in Crohn 's disease and experimental colitis
EMTREE CODES:
...10; J2.10; A10; J2.30.30; A11; J2.30.5; L1; J1.100; J1;
D4.680.265.60.680 ; D4.270; D24.35.880; G3.560.560.460.350.880...

14/6,KWIC/11 (Item 11 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11934446 EMBASE No: 2003045097
From extracellular to intracellular targets, inhibiting MAP kinases in treatment of Crohn 's disease
2002

From extracellular to intracellular targets, inhibiting MAP kinases in treatment of Crohn 's disease
EMTREE CODES:
...G3.180; J2.20.10; B2.60.60.60.10.40; J2.20; J1.200; **D4.680.265.60.680** ;
D4.270; D29.275.60.680.700.540; E5.680.210...

14/6,KWIC/12 (Item 12 from file: 73)

DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11932228 EMBASE No: 2003042724
Biological therapy to Crohn 's disease with anti-tumor necrosis factor alpha
01 JAN 2003

Biological therapy to Crohn 's disease with anti-tumor necrosis factor alpha
EMTREE CODES:
...750; D4.830; D22.37.710; D29.50.710; D2.20.50.20.10.720;
D4.680.265.60.680 ; D20.30.440; D24.35.190.440; D4.680.190.440...

14/6,KWIC/13 (Item 13 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11898850 EMBASE No: 2003010683
Genetic dissection of the cellular pathways and signaling mechanisms in modeled tumor necrosis factor-induced Crohn 's-like inflammatory bowel disease
16 DEC 2002

Genetic dissection of the cellular pathways and signaling mechanisms in modeled tumor necrosis factor-induced Crohn 's-like inflammatory bowel disease
EMTREE CODES:
...D4.680.190.440; D4.680; D4.680.140.750.190; G3.880.750.190;
D4.680.265.60.680 ; D4.680.265.60.630

14/6,KWIC/14 (Item 14 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11871280 EMBASE No: 2002444410
Pharmacogenomics of response to anti-tumor necrosis factor therapy in patients with Crohn 's disease
2002

Pharmacogenomics of response to anti-tumor necrosis factor therapy in patients with Crohn 's disease
EMTREE CODES:
...190; D4.680.190; D4.270; D4.680.140.750.190; G3.880.750.190;
D4.680.265.60.680 ; D24.35.880; G3.560.560.460.350.880; D4.680...

14/6,KWIC/15 (Item 15 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11838118 EMBASE No: 2002410807
Treatment of Crohn 's disease - The new era
01 OCT 2002

Treatment of Crohn 's disease - The new era
EMTREE CODES:
...20.50.20.50.200; D4.635.640.190; D29.275.60.680.700.540;
D4.680.265.60.680 ; D40; D4.635.630.75.535; D1.20.230

14/6,KWIC/16 (Item 16 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11818334 EMBASE No: 2002384027
Inflammatory signal transduction in Crohn 's disease and novel **therapeutic approaches**
01 SEP 2002

Inflammatory signal transduction in Crohn **'s disease and novel therapeutic approaches**
EMTREE CODES:
...470; A13; E5.345.345.345.930; G3.560.560.470.930; J1.100; J1; **D4.680.265.60.680** ; D24.35.190.750; D4.680.190.750; D4.680.750...

14/6,KWIC/17 (Item 17 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11726935 EMBASE No: 2002299548
Anti-tumour necrosis factor therapy in Crohn **'s disease: Where are we now?**
2002

Anti-tumour necrosis factor therapy in Crohn **'s disease: Where are we now?**
EMTREE CODES:
...660.700; D2.30.90.410.400.780; D9.20; D2.30.90.40.45; **D4.680.265.60.680**

14/6,KWIC/18 (Item 18 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11623224 EMBASE No: 2002194257
How I treat a patient with corticosteroid-dependent Crohn **'s disease?**
2002

How I treat a patient with corticosteroid-dependent Crohn **'s disease?**
EMTREE CODES:
...750.190; D14.30.500; D2.30.50.30.10; D2.30.50.40.45; **D4.680.265.60.680** ; D4.635.640.700; D20.30; D24.15.140.490.510...

14/6,KWIC/19 (Item 19 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11449767 EMBASE No: 2002021539
Inhibition of stress-activated MAP kinases induces clinical improvement in moderate to severe Crohn **'s disease**
2002

Inhibition of stress-activated MAP kinases induces clinical improvement in moderate to severe Crohn **'s disease**
EMTREE CODES:
...50.280; J2.10; J2.50; A10; J2.30.30; A11; L1; J1.100; J1; **D4.680.265.60.680** ; D4.270; D14.30.500; C6.425.40; E5.20.240...

14/6,KWIC/20 (Item 20 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

11401628 EMBASE No: 2001416407
Monocytes or T cells in Crohn 's disease: Does IL-16 allow both to play at that game?
2001

Monocytes or T cells in Crohn 's disease: Does IL-16 allow both to play at that game?
EMTREE CODES:
...15.140.490.510; D4.65.140.490.510; G2.440.40.140.490.510; **D4.680.265.60.680** ; G3.560.560.320; D4.680; D4.140.490; D1.20...

14/6,KWIC/21 (Item 21 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

07157412 EMBASE No: 1998046633
Severe muscle damage induced by high carbohydrate intake from elemental diet in a patient with Crohn 's disease
1998

Severe muscle damage induced by high carbohydrate intake from elemental diet in a patient with Crohn 's disease
EMTREE CODES:
...60.10.40; J2.20.10; L2.20; J2.40.10; L1; J1.100; J1; **D4.680.265.60.680** ; D4.270; D4.140.140.700

14/6,KWIC/22 (Item 22 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

06609325 EMBASE No: 1996274098
Polymyositis, alopecia universalis, and primary sclerosing cholangitis in a patient with Crohn 's disease
1996

Polymyositis, alopecia universalis, and primary sclerosing cholangitis in a patient with Crohn 's disease
EMTREE CODES:
...345; D4.680.700; D4.830.830.170; D6.40.80.20; C6.425.40; **D4.680.265.60.680** ; D4.680.265.60.20

14/6,KWIC/23 (Item 23 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

06198559 EMBASE No: 1995199516
Functional and morphological changes in small bowel of Crohn 's disease patients. Influence of site of disease
1995

Functional and morphological changes in small bowel of Crohn 's disease patients. Influence of site of disease
EMTREE CODES:

...260.490.160; L2.60; G1.580; J1; D4.680.265.10.350; D4.270;
D4.680.265.60.680

14/6,KWIC/24 (Item 24 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

05599597 EMBASE No: 1994002731
Dermatomyositis associated with Crohn **'s disease**
1994

Dermatomyositis associated with Crohn **'s disease**
EMTREE CODES:
...40; D24.440.445; E2.230.225; D4.830.830.170; D6.40.80.20;
D4.680.265.60.680 ; D4.270

14/6,KWIC/25 (Item 25 from file: 73)
DIALOG(R)File 73:(c) 2005 Elsevier Science B.V. All rts. reserv.

03452739 EMBASE No: 1987205316
Rhabdomyolysis associated with Crohn **'s disease**
1987

Rhabdomyolysis associated with Crohn **'s disease**
EMTREE CODES:
D4.680.265.60.680 ; C2.220.227.260.160; C2.220.260.260.160; C2...
? logoff hold
10aug05 08:43:22 User228206 Session D2488.4
$3.56 1.048 DialUnits File155
$0.84 4 Type(s) in Format 9
$0.84 4 Types
$4.40 Estimated cost File155
$7.21 1.222 DialUnits File5
$12.00 6 Type(s) in Format 9
$12.00 6 Types
$19.21 Estimated cost File5
$12.92 0.584 DialUnits File34
$6.43 1 Type(s) in Format 9
$6.43 1 Types
$19.35 Estimated cost File34
$0.25 0.061 DialUnits File35
$0.25 Estimated cost File35
$0.26 0.048 DialUnits File48
$0.26 Estimated cost File48
$0.32 0.085 DialUnits File65
$0.32 Estimated cost File65
$2.92 0.333 DialUnits File71
$2.92 Estimated cost File71
$13.89 1.307 DialUnits File73
$0.00 28 Type(s) in Format 6
$2.94 1 Type(s) in Format 9
$8.75 25 Type(s) in Format 95 (KWIC)
$11.69 54 Types
$25.58 Estimated cost File73
$0.22 0.050 DialUnits File91
$0.22 Estimated cost File91
$2.23 0.638 DialUnits File94
$2.23 Estimated cost File94

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          $0.30    0.070 DialUnits File98
      $0.30  Estimated cost File98
          $0.55    0.102 DialUnits File135
      $0.55  Estimated cost File135
          $3.69    0.821 DialUnits File144
      $3.69  Estimated cost File144
          $0.89    0.203 DialUnits File149
      $0.89  Estimated cost File149
          $1.34    0.227 DialUnits File156
      $1.34  Estimated cost File156
          $0.91    0.287 DialUnits File159
      $0.91  Estimated cost File159
          $0.80    0.179 DialUnits File162
      $0.80  Estimated cost File162
          $0.14    0.039 DialUnits File164
      $0.14  Estimated cost File164
          $0.51    0.048 DialUnits File172
      $0.51  Estimated cost File172
          $0.25    0.070 DialUnits File266
             $1.90  1 Type(s) in Format  9
          $1.90  1 Types
      $2.15  Estimated cost File266
          $0.11    0.033 DialUnits File369
      $0.11  Estimated cost File369
          $0.10    0.028 DialUnits File370
      $0.10  Estimated cost File370
          $6.42    0.512 DialUnits File399
             $8.25  3 Type(s) in Format  9
          $8.25  3 Types
     $14.67  Estimated cost File399
          $2.89    0.131 DialUnits File434
      $2.89  Estimated cost File434
          $0.30    0.063 DialUnits File444
      $0.30  Estimated cost File444
          $0.21    0.033 DialUnits File467
      $0.21  Estimated cost File467
          OneSearch, 26 files,  8.219 DialUnits FileOS
      $1.33  TELNET
    $105.63  Estimated cost this search
    $105.63  Estimated total session cost   8.219 DialUnits

Logoff: level 05.06.01 D  08:43:22

You are now logged off
```

11/9/6 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014521391 BIOSIS NO.: 200300475346
Role of PYK2 **in cell adhesion of human prostate** cancer **cells.**
AUTHOR: Yuan Ta-Chun (Reprint); Lee Ming-Shyue (Reprint); Mehta Parmender P (Reprint); Lin Ming-Fong (Reprint)
AUTHOR ADDRESS: University of Nebraska Medical Center, Omaha, NE, USA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 44 p813 July 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 94th Annual Meeting of the American Association for Cancer Research Washington, DC, USA July 11-14, 2003; 20030711
ISSN: 0197-016X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 144114-16-9: focal adhesion kinase; 80449-02-1: focal adhesion kinase
ENZYME COMMISSION NUMBER: EC 2.7.1.112: focal adhesion kinase
DESCRIPTORS:
MAJOR CONCEPTS: Cell Biology; Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: LNCaP cell line (Hominidae); MDA PCa2b cell line (Hominidae)
ORGANISMS: PARTS ETC: cytoplasm; nucleus
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: prostate cancer--neoplastic disease, reproductive system disease/male, urologic disease
MESH TERMS: Prostatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: cDNA {complementary DNA}; focal adhesion kinase; pY402; proline-rich kinase 2--expression
MISCELLANEOUS TERMS: cell adhesion; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02502 Cytology - General
02508 Cytology - Human
10062 Biochemistry studies - Nucleic acids, purines and pyrimidines
10802 Enzymes - General and comparative studies: coenzymes
15506 Urinary system - Pathology
16506 Reproductive system - Pathology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
BIOSYSTEMATIC CODES:
86215 Hominidae

11/9/7 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013801386 BIOSIS NO.: 200200394897
CaSm mediated transformation of pancreatic and lung cancer : Pyk2 **is a downstream effector**
AUTHOR: Hubbard Joshua M (Reprint); Jones Ned T (Reprint); Boylan Alice M (Reprint); Watson Dennis K (Reprint); Cole David J (Reprint)
AUTHOR ADDRESS: Hollings Cancer Center, Medical University of South

Carolina, Charleston, SC, USA**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 43 p357-358 March, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 93rd Annual Meeting of the American Association for Cancer Research San Francisco, California, USA April 06-10, 2002; 20020406
ISSN: 0197-016X
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Digestive System--Ingestion and Assimilation; Molecular Genetics--Biochemistry and Molecular Biophysics; Respiratory System--Respiration; Tumor Biology
BIOSYSTEMATIC NAMES: Adenoviridae--dsDNA Viruses, Viruses, Microorganisms ; Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: adenovirus (Adenoviridae)--gene vector; A549 cell line (Hominidae)--human lung cancer cell, proliferation; ASPC1 cell line (Hominidae)--human pancreatic cancer cell, proliferation; BXPC3 cell line (Hominidae)--human pancreatic cancer cell, proliferation; CRL5808 cell line (Hominidae)--human lung cancer cell, proliferation; CRL5895 cell line (Hominidae)--human lung cancer cell, proliferation; Panc1 cell line (Hominidae)--human pancreatic cancer cell, proliferation; W138 cell line (Hominidae); human (Hominidae)--patient
COMMON TAXONOMIC TERMS: Double-Stranded DNA Viruses; Microorganisms; Viruses; Animals; Chordates; Humans; Mammals; Primates; Vertebrates
DISEASES: lung cancer--neoplastic disease, respiratory system disease, genetics; pancreatic cancer--digestive system disease, neoplastic disease, genetics
MESH TERMS: Lung Neoplasms (MeSH); Pancreatic Neoplasms (MeSH)
CHEMICALS & BIOCHEMICALS: GFP {green fluorescent protein}; RNA; cancer associated Sm-like protein {CaSm}; protein tyrosine kinase 2 {Pyk2}--downstream effector; protein tyrosine kinase 2 mRNA {protein tyrosine kinase 2 messenger RNA}
GENE NAME: human CaSM gene (Hominidae) {human cancer associated Sm-like protein gene}--expression, oncogene; human Pyk2 gene (Hominidae) { human protein tyrosine kinase 2 gene}--expression, regulation
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02508 Cytology - Human
03502 Genetics - General
03508 Genetics - Human
10062 Biochemistry studies - Nucleic acids, purines and pyrimidines
10064 Biochemistry studies - Proteins, peptides and amino acids
14004 Digestive system - Physiology and biochemistry
14006 Digestive system - Pathology
16004 Respiratory system - Physiology and biochemistry
16006 Respiratory system - Pathology
24004 Neoplasms - Pathology, clinical aspects and systemic effects
31500 Genetics of bacteria and viruses
33506 Virology - Animal host viruses
BIOSYSTEMATIC CODES:
03116 Adenoviridae
86215 Hominidae

11/9/8 (Item 4 from file: 5)

0013739035 BIOSIS NO.: 200200332546

Overexpression of proline-rich tyrosine kinase PYK2 **induces apoptosis in small cell lung** cancer **cells**

AUTHOR: Chubanov V; Roelle S; Stoeppler H; Gudermann T (Reprint)
AUTHOR ADDRESS: Institut fuer Pharmakologie und Toxikologie, Philipps-Universitaet Marburg, Karlvon-Frisch-Str.1, 35033, Marburg, Germany**Germany

JOURNAL: Naunyn-Schmiedeberg's Archives of Pharmacology 365 (Supplement 1): pR22 March, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 43rd Spring Meeting of the German Society for Experimental and Clinical Pharmacology and Toxicology Mainz, Germany March 12-14, 2002; 20020312
ISSN: 0028-1298
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 58-82-2: bradykinin; 7440-70-2: calcium; 142243-02-5: extracellular signal-regulated kinase; 119418-04-1: galanin; 56092-81-0 : ionomycin; 141436-78-4: protein kinase C

DESCRIPTORS:
- MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Cell Biology; Reproductive System--Reproduction; Tumor Biology
- BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Retroviridae--DNA and RNA Reverse Transcribing Viruses, Viruses, Microorganisms
- ORGANISMS: PC12 cell line (Muridae); retrovirus (Retroviridae)--gene vector
- ORGANISMS: PARTS ETC: neuronal tissue
- COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrates; DNA and RNA Reverse Transcribing Viruses; Microorganisms; Viruses
- DISEASES: small cell lung cancer--neoplastic disease, respiratory system disease
- MESH TERMS: Carcinoma, Small Cell (MeSH); Lung Neoplasms (MeSH)
- CHEMICALS & BIOCHEMICALS: G protein-coupled receptors; PYK2--calcium-dependent tyrosine kinase, expression, proline-rich; bombesin/gastrin-releasing peptide (GRP)--autocrine effects, paracrine effects; bradykinin--autocrine effects, paracrine effects; calcium--intracellular concentration; extracellular signal-regulated kinase (ERK)--regulation; galanin--autocrine effects, paracrine effects; ionomycin--calcium-ionophore; neuropeptide receptors; protein kinase C
- METHODS & EQUIPMENT: bisbenzimide staining--analytical method, staining method; fluorescent microscopy--analytical method, microscopy method
- MISCELLANEOUS TERMS: apoptosis; cell death; cell proliferation; enzyme activity; metastatic potential; Meeting Abstract; Meeting Abstract

CONCEPT CODES:
- 00520 General biology - Symposia, transactions and proceedings
- 02502 Cytology - General
- 02506 Cytology - Animal
- 10060 Biochemistry studies - General
- 10064 Biochemistry studies - Proteins, peptides and amino acids
- 10069 Biochemistry studies - Minerals
- 10802 Enzymes - General and comparative studies: coenzymes
- 16006 Respiratory system - Pathology
- 16504 Reproductive system - Physiology and biochemistry

24004 Neoplasms - Pathology, clinical aspects and systemic effects
33506 Virology - Animal host viruses
BIOSYSTEMATIC CODES:
86375 Muridae
03305 Retroviridae

11/9/9 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012759732 BIOSIS NO.: 200000478045
Galanin-mediated activation of PYK2 and Src tyrosine kinases promotes growth of small cell lung cancer cells
AUTHOR: Roelle S (Reprint); Grosse R (Reprint); Hofmann T (Reprint); Schultz G; Gudermann T (Reprint)
AUTHOR ADDRESS: Institut fuer Pharmakologie und Toxikologie, Philipps-Universitaet Marburg, Marburg, Germany**Germany
JOURNAL: Naunyn-Schmiedeberg's Archives of Pharmacology 362 (4-5 Supplement): pR20 2000 2000
MEDIUM: print
CONFERENCE/MEETING: ANPT-Symposium Berlin-Dahlem, Germany September 27, 200020000927
SPONSOR: German Society for Experimental and Clinical Pharmacology and Toxicology
ISSN: 0028-1298
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 141349-89-5: Src tyrosine kinases; 119418-04-1: galanin
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Respiratory System --Respiration; Tumor Biology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: H510 cell line (Hominidae)--small cell lung cancer cells; H69 cell line (Hominidae)--small cell lung cancer cells
COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates
CHEMICALS & BIOCHEMICALS: PYK2--galanin-mediated activation; Src tyrosine kinases--galanin-mediated activation; galanin
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
10064 Biochemistry studies - Proteins, peptides and amino acids
00520 General biology - Symposia, transactions and proceedings
02508 Cytology - Human
10060 Biochemistry studies - General
16004 Respiratory system - Physiology and biochemistry
24004 Neoplasms - Pathology, clinical aspects and systemic effects
BIOSYSTEMATIC CODES:
86215 Hominidae

11/9/10 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012557460 BIOSIS NO.: 200000275773
RAFTK/ PYK2 tyrosine kinase mediates the association of P190 RhoGAP with

Jones C.
Breast Cancer Research (BREAST CANCER RES.) (United Kingdom) 2000, 2/4 (298-299)
CODEN: BCRRC ISSN: 1465-5411
DOCUMENT TYPE: Journal ; Note
LANGUAGE: ENGLISH
DRUG DESCRIPTORS:
*protein tyrosine kinase--endogenous compound--ec
phosphatidylinositol 3 kinase--endogenous compound--ec; mitogen activated protein kinase--endogenous compound--ec; actin--endogenous compound--ec; guanosine triphosphatase activating protein--endogenous compound--ec; Ras protein--endogenous compound--ec; unclassified drug
MEDICAL DESCRIPTORS:
*signal transduction; *breast cancer
cancer cell; cell invasion; oncogene neu; gene overexpression; prognosis; drug targeting; cell migration; cytoskeleton; human; human cell; note
DRUG TERMS (UNCONTROLLED): related adhesion focal tyrosine kinase --endogenous compound--ec
CAS REGISTRY NO.: 80449-02-1 (protein tyrosine kinase); 115926-52-8 (phosphatidylinositol 3 kinase); 142243-02-5 (mitogen activated protein kinase)
SECTION HEADINGS:
016 Cancer
029 Clinical and Experimental Biochemistry

11/9/13 (Item 1 from file: 266)
DIALOG(R)File 266:FEDRIP

00581827
IDENTIFYING NO.: 5R21CA102998-02 AGENCY CODE: CRISP
PYK2 **& Therapeutic Strategies-** Cancer **-induced Osteolysis**
PRINCIPAL INVESTIGATOR: LI, RONGBAO
ADDRESS: LI@SRI.ORG SOUTHERN RESEARCH INSTITUTE 2000 NINTH AVENUE SOUTH BIRMINGHAM, AL 35205
PERFORMING ORG.: SOUTHERN RESEARCH INSTITUTE, BIRMINGHAM, ALABAMA
SPONSORING ORG.: NATIONAL CANCER INSTITUTE
DATES: 2009/10/03 TO 2008/31/05 FY : 2004 TYPE OF AWARD: Noncompeting Continuation (Type 5)
SUMMARY: DESCRIPTION (provided by applicant): Common cancers, such as those of the breast, prostate and lung, frequently metastasize to bone and lead to bone disorder and untreatable consequences. Bone metastases contribute heavily to morbidity and mortality. About 75% of patients with advanced breast carcinoma developed significant tumor burden in the skeleton and resulted in severe bone osteolytic lesions. Current understanding of the molecular mechanism of bone metastasis is limited, however, studies indicate that bone microenvironment plays a role in osteolytic metastasis and involves a coupling between osteolysis and cancer cell growth through interactions between the tumor cells and the bone-resorbing osteoclasts. Proline-rich tyrosine kinase (PYK2), a cellular adhesion kinase, is expressed in high levels in osteoclasts and plays an important role in the adhesion-dependent, integrin-mediated signaling that leads to cytoskeletal reorganization and formation of the sealing zone during osteoclast activation. Autophosphorylation of PYK2 and interactions with Src kinase and CAS, a docking protein for SH2 and SH3-containg molecules, is required for the signaling. However, little is known concerning the molecular mechanism by which PYK2 regulates osteoclast function. Our long-term research goal is to understand the structural

biology and function of PYK2 in osteoclast activation, explore the relationship among its structure, function, and dynamics, and exploit this relation for the design of specific inhibitors that alter PYK2's function required for osteolysis. Towards this goal, we will determine the structure of PYK2 in complex with substrate analogs and interacting protein domains. We hypothesize that interruption of this signaling pathway by inhibition of PYK2 activity prevents osteoclast activation and eventually disrupts the vicious cycle of osteolysis and cancer cell growth. Through a combination of structure and activity-based approaches, we will identify candidate leads of PYK2 specific inhibitors which not only serve as a probe to test this hypothesis and further study the mechanism by which PYK2 acts in osteoclast activation, but also lead to a potential therapeutic agent for cancer-induced bone resorption. We propose a comprehensive and collaborative effort by focusing initially on the following specific aims: 1) to express and purify active PYK2 in full length and separate domains, to characterize the kinase activity and binding activity of PYK2 with the SH2 domain of Src and the SH3 domain of CAS; 2) to crystallize PYK2 and determine the three-dimensional structure of PYK2 and its domains; 3) to use a combination of structure- and cellular activity-based approaches to identify candidate leads of specific PYK2 inhibitors that target the PYK2 kinase domain, possibly the protein-protein interactions that are required for its function in osteoclast activation.

DESCRIPTORS: biological signal transduction; cell cycle; X ray crystallography; enzyme inhibitor; enzyme structure; osteoclast activating factor; bone neoplasm; protein tyrosine kinase; crystallization; protein purification; cell adhesion molecule; integrin; pathologic bone resorption; osteoclast; enzyme activity; surface plasmon resonance; protein protein interaction

11/9/14 (Item 1 from file: 399)

DIALOG(R)File 399:CA SEARCH(R)

133103737 CA: 133(8)103737q PATENT

PYK2 (RAFTK) and inflammation

INVENTOR(AUTHOR): Schlessinger, Joseph; Kigaki, Mitsuhiko; Gishizky, Mikhail

LOCATION: USA

ASSIGNEE: Sugen, Inc.

PATENT: PCT International ; WO 200040971 A1 DATE: 20000713

APPLICATION: WO 98US27871 (19981231)

PAGES: 84 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: G01N-335/73; G01N-033/68; G01N-033/86; G01N-335/66; C12Q-001/48; C12N-009/12

DESIGNATED COUNTRIES: AL; AT; AU; AZ; BG; BR; CA; CH; CN; CZ; DE; DK; FI; GB; GH; HR; HU; IL; IS; JP; KR; LC; LK; LR; LT; LU; LV; MD; NO; NZ; PL; RU; SE; US; YU DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD; SZ; UG; AT; BE; DE ; DK; FI; FR; GB; IE; IT; LU; PT; BF; BJ; GA; GN; ML; MR; NE; SN; TD; TG

SECTION:

CA215008 Immunochemistry

CA201XXX Pharmacology

CA203XXX Biochemical Genetics

CA263XXX Pharmaceuticals

IDENTIFIERS: nonreceptor tyrosine kinase PYK2 RAFTK inflammation, drug screening PYK2 RAFTK antiinflammatory agent

DESCRIPTORS:

Influenza virus...

airway inflammation model; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related

diseases
Intestine,disease...
diseases; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Animal cell...
disease model; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Connective tissue...
disease; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Respiratory tract...
inflammation; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Intestine,disease...
inflammatory; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Connective tissue...
mixed connective tissue disease; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Disease models...
mouse and cellular; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Drug delivery systems... Drug screening... Inflammation... Mammal(Mammalia) ... Organic compounds,biological studies... Peptidomimetics... Rheumatoid arthritis... Signal transduction,biological... Sjogren's syndrome... Tumor necrosis factors...
non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Cytokines...
prodn.; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Dephosphorylation,biological... Phosphorylation,biological...
PYK2 and binding partner; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Mouse...
PYK2 gene-knockout; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Gene,animal...
pyk2; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Connective tissue...
scleroderma; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Anti-inflammatory agents...
screening; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Lupus erythematosus...
systemic; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Cytotoxic agents...
tyrphostins; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
Intestine,disease...
ulcerative colitis; non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases

CAS REGISTRY NUMBERS:

91-22-5 biological studies, non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related

diseases
59-48-3D 91-19-0D 3260-61-5D derivs., non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
253-82-7 170780-46-8 non-receptor tyrosine kinase PYK2 and inflammation and screening of therapeutic for inflammation-related diseases
283620-47-3 283620-48-4 283620-49-5 283620-50-8 283620-51-9 unclaimed nucleotide sequence; pYK2 (RAFTK) and inflammation

11/9/15 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

129064594 CA: 129(6)64594m PATENT
PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
INVENTOR(AUTHOR): Lev, Simma; Schlessinger, Joseph
LOCATION: USA
ASSIGNEE: Sugen, Inc.; New York University Medical Center; Lev, Simma; Schlessinger, Joseph
PATENT: PCT International ; WO 9826054 A2 DATE: 19980618
APPLICATION: WO 97US22565 (19971209) *US 32824 (19961211)
PAGES: 86 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-009/12A; C12N-015/12B; C12N-015/63B; C12N-001/21B; C12N-001/19B; C12N-005/10B
DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD ; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA206001 General Biochemistry
CA201XXX Pharmacology
CA203XXX Biochemical Genetics
IDENTIFIERS: sequence PYK2 protein tyrosine kinase cDNA, signal transduction PYK2 disease drug diagnosis
DESCRIPTORS:
Pain...
acute/chronic; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
cDNA sequences...
for PYK2 protein tyrosine kinase of human
Lipoproteins...
gene src; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
Receptors...
Gi or Gq protein-coupled; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
Hyperkinesia...
in children; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
Drugs...

indolinones; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
Protein sequences...
of PYK2 protein tyrosine kinase of human
Alzheimer's disease... Diagnosis... Epilepsy... Grb2 protein...
Lysophosphatidic acids... Migraine... Neurodegenerative diseases...
Parkinson's disease... Phosphorylation(biological)... Schizophrenia... SHC protein... Signal transduction(biological)... Stroke...
PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
Genetic vectors...
PYK2-encoding; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
Cell(biological)...
PYK2-expressing; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
G proteins(guanine nucleotide-binding proteins)...
Sos1; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
CAS REGISTRY NUMBERS:
209055-80-1 209055-84-5 209055-87-8 209055-89-0 209055-91-4 209055-92-5 209055-95-8 209055-97-0 amino acid sequence, nucleotide encoding; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
170781-87-0 amino acid sequence; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
208999-05-7 208999-06-8 nucleotide encoding; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
168882-46-0 nucleotide sequence; PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases
58-82-2 170780-46-8 PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases

11/9/16 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

125105146 CA: 125(9)105146e PATENT
Protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, especially neurological diseases
INVENTOR(AUTHOR): Lev, Sima; Schlessinger, Joseph
LOCATION: USA
ASSIGNEE: Sugen, Inc.; New York University
PATENT: PCT International ; WO 9618738 A2 DATE: 960620
APPLICATION: WO 95US15846 (951206) *US 357642 (941215) *US 460626 (950602)

PAGES: 139 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-015/54A; C12N-009/12B; C12Q-001/68B; C07K-016/40B; C12N-005/12B; G01N-033/68B; C12Q-001/48B; C07D-041/40B; C07C-255/34B; C07D-215/00B; C07D-239/72B

DESIGNATED COUNTRIES: AM; AT; AU; BB; BG; BR; BY; CA; CH; CN; CZ; DE; DK; EE; ES; FI; GB; GE; HU; IS; JP; KE; KG; KP; KR; KZ; LK; LR; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; TJ; TM

DESIGNATED REGIONAL: KE; LS; MW; SD; SZ; UG; AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG

SECTION:
CA201011 Pharmacology
CA203XXX Biochemical Genetics
CA207XXX Enzymes
CA213XXX Mammalian Biochemistry
CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: protein tyrosine kinase PYK2 sequence human, cDNA protein tyrosine kinase sequence human, gene therapy PYK2 kinase neurol disease, diagnosis neurol disease PYK2 kinase gene, signal transduction disease PYK2 kinase

DESCRIPTORS:
Phosphoproteins,SHC... Proteins,specific or class, Grb-2...
assocn. with PYK2; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Genetic element,promoter... Genetic element,terminator...
expression vector; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Developmental stages,child...
extreme hyperactivity; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Hyperkinesia...
extreme, in children; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Proteins,specific or class, potassium channel-forming...
Kv1.2, phosphorylation in response to PYK2 activation; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol.
Biological transport,influx... Electric activity,depolarization...
membrane depolarization, calcium influx, and PYK2 phosphorylation; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, e
Antibodies... Brain,disease, stroke... Deoxyribonucleic acid sequences,complementary... Diagnosis... Epilepsy... Genetic vectors... Headache,migraine... Mental disorder,Alzheimer's disease... Molecular cloning... Nervous system,disease, degeneration... Nucleotides,oligo-, probes... Pain,acute... Pain,chronic... Parkinsonism... Phosphorylation,biological... Protein sequences... Schizophrenia... Signal transduction,biological... Therapeutics,geno-...
protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Cytotoxic agents,tyrphostins...
PYK2 inhibitor; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Gene...
PYK2-encoding; protein tyrosine kinase PYK2 cDNA sequence, cloning, and

use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
Disease...
PYK2-mediated signal transduction; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
G proteins(guanine nucleotide-binding proteins)...
SOS-1, assocn. with PYK2; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
CAS REGISTRY NUMBERS:
142243-02-5 activation by bradykinin; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
170781-87-0P amino acid sequence; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
7440-70-2 biological studies, membrane depolarization, calcium influx, and PYK2 phosphorylation; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
51-84-3 biological studies, PYK2 activator; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
91-22-5 biological studies, PYK2 inhibitor; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
51-83-2 MAP kinase activator; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
168882-46-0 nucleotide sequence; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
58-82-2 PYK2 activator; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
91-19-0 253-82-7 PYK2 inhibitor; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
80449-02-1P 2; protein tyrosine kinase PYK2 cDNA sequence, cloning, and use in diagnosis and gene therapy of signal transduction-related diseases, esp. neurol. diseases
? ds

Set	Items	Description
S1	3335	E3-E50
S2	86	'FOCAL ADHESION KINASE 2'
S3	173883	'FOCAL ADHESION KINASE 2' OR DC='D4.680.265.60.680' OR R4:-R10
S4	176858	S1 OR S2 OR S3
S5	90232	S4 AND (INCREASE? OR DECREASE? OR REDUC? OR HIGHER? OR LOWER? OR INSUFFIC? OR DEPLET? OR DEFICIENT?)
S6	32420	S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)
S7	4690	S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)/TI
S8	43	S4/TI (100N) (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)
S9	2437	S4 AND ((CONNECTIVE? (3N) TISSUE?) OR ARTHRIT? OR DEGENERATIV?)

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1951-2005/Aug W1
         (c) format only 2005 Dialog
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         (c) 2005 Inst for Sci Info
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  File 135:NewsRx Weekly Reports 1995-2005/Jul W5
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*File 135: New newsletters are now added. See Help News135 for the
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  File 149:TGG Health&Wellness DB(SM) 1976-2005/Jul W5
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  File 156:ToxFile 1965-2005/Aug W1
         (c) format only 2005 Dialog
*File 156: ToxFile has been reloaded with the 2005 MeSH.
Please see HELP NEWS 156 for details.
  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
*File 159: Cancerlit is no longer updating.
Please see HELP NEWS159.
  File 162:Global Health 1983-2005/Jul
         (c) 2005 CAB International
  File 164:Allied & Complementary Medicine 1984-2005/Aug
         (c) 2005 BLHCIS
  File 172:EMBASE Alert 2005/Aug 10
         (c) 2005 Elsevier Science B.V.
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  File 369:New Scientist 1994-2005/May W5
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  File 370:Science 1996-1999/Jul W3
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information.
  File 399:CA SEARCH(R) 1967-2005/UD=14307
         (c) 2005 American Chemical Society
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  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
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  File 444:New England Journal of Med. 1985-2005/Jul W4
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*File 467: F467 no longer updates; see Help News467. 7.

Set	Items	Description

Cost is in DialUnits
? t s22/9/30 29 18 21 25

Set	Items	Description
S1	3335	E3-E50
S2	86	'FOCAL ADHESION KINASE 2'
S3	173883	'FOCAL ADHESION KINASE 2' OR DC='D4.680.265.60.680' OR R4:-R10
S4	176858	S1 OR S2 OR S3
S5	90232	S4 AND (INCREASE? OR DECREASE? OR REDUC? OR HIGHER? OR LOWER? OR INSUFFIC? OR DEPLET? OR DEFICIENT?)
S6	32420	S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)
S7	4690	S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)/TI
S8	43	S4/TI (100N) (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR CROHN? OR COLITIS?)
S9	2437	S4 AND ((CONNECTIVE? (3N) TISSUE?) OR ARTHRIT? OR DEGENERATIV?)
S10	43	S8
S11	16	RD (unique items)
S12	182	S4 AND ARTHRIT?/TI
S13	28	S4 AND COLITIS?/TI
S14	25	S4 AND CROHN?/TI
S15	6175059	REVIEW? OR TUTOR?
S16	17720	S15 AND S4
S17	12	S4/TI AND (DISEASE? OR COLLAGEN? OR ARTHRITIS? OR COLITIS? OR CROHN? OR INFLAMMAT?)/TI
S18	108	S4 (5N) LEVEL?
S19	71	S18 (25N)(INCREASE? OR DECREASE? OR HIGHER? OR LOWER? OR IMBALANCE? OR DIMINISH? OR REDUC?)
S20	25	RD (unique items)
S21	31	S4 AND INDOLINONE?
S22	31	RD (unique items)

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22/9/30 (Item 30 from file: 73)
DIALOG(R)File 73:EMBASE
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06864215 EMBASE No: 1997148537
Structures of the tyrosine kinase domain of fibroblast growth factor receptor in complex with inhibitors
Mohammadi M.; McMahon G.; Sun L.; Tang C.; Hirth P.; Yeh B.K.; Hubbard S.R.; Schlessinger J.
S.R. Hubbard, Department of Pharmacology, Skirball Inst. of Biomolecular Med., New York University Medical Center, New York, NY 10016 United States
Science (SCIENCE) (United States) 1997, 276/5314 (955-960)
CODEN: SCIEA ISSN: 0036-8075
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

A new class of protein tyrosine kinase inhibitors was identified that is based on an oxindole core (indolinones). Two compounds from this class inhibited the kinase activity of fibroblast growth factor receptor 1 (FGFR1) and showed differential specificity toward other receptor tyrosine kinases. Crystal structures of the tyrosine kinase domain of FGFR1 in complex with the two compounds were determined. The oxindole occupies the site in which the adenine of adenosine triphosphate binds, whereas the moieties that extend from the oxindole contact residues in the hinge region between the two kinase lobes. The more specific inhibitor of FGFR1 induces a conformational change in the nucleotide-binding loop. This structural information will facilitate the design of new inhibitors for use in the treatment of cancer and other diseases in which cell signaling by tyrosine kinases plays a crucial role in disease pathogenesis.

DRUG DESCRIPTORS:
*fibroblast growth factor receptor; *protein tyrosine kinase
MEDICAL DESCRIPTORS:
*protein structure
article; enzyme activity; priority journal; protein binding; protein domain ; signal transduction; structure activity relation; structure analysis
CAS REGISTRY NO.: 80449-02-1 (protein tyrosine kinase)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

22/9/29 (Item 29 from file: 73)
DIALOG(R)File 73:EMBASE

07221126 EMBASE No: 1998120483
Tyrosine kinases in disease: Overview of kinase inhibitors as therapeutic agents and current drugs in clinical trials
Strawn L.M.; Shawver L.K.
L.M. Strawn, SUGEN Inc., 351 Galveston Drive, Redwood City, CA 94063 United States
Expert Opinion on Investigational Drugs (EXPERT OPIN. INVEST. DRUGS) (United Kingdom) 1998, 7/4 (553-573)
CODEN: EOIDE ISSN: 1354-3784
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 190

Tyrosine kinases, first described as oncogenes, have been shown to play a role in normal cellular processes. Aberrations in tyrosine kinase activity lead to disease states. For fifteen years it has been postulated that the inhibition of tyrosine kinases may have therapeutic utility and the design and testing of inhibitors have been major focuses of research and development in both academic institutions and pharmaceutical companies. While early research focused on developing chemical entities that mimic phosphotyrosine, later research has focused on developing competitive adenosine triphosphate (ATP) inhibitors with various levels of selectivity on kinase targets. This review focuses on a discussion of tyrosine kinases thought to be important in disease, including platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), vascular endothelial cell growth factor (VEGF), epidermal growth factor (EGF) receptors, HER-2 and Src. In addition, the classes of inhibitors designed to affect these targets and that have overcome research and development challenges and entered clinical trials are discussed. These include isoxazole, quinazoline, substituted pyrimidines and indolinone compounds, all of which

22/3,KWIC/31 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

129064594 CA: 129(6)64594m PATENT

PYK2 protein tyrosine kinase, screening for drugs for treatment of PYK2 signal transduction-related diseases, and methods for diagnosis of such diseases

INVENTOR(AUTHOR): Lev, Simma; Schlessinger, Joseph
LOCATION: USA
ASSIGNEE: Sugen, Inc.; New York University Medical Center; Lev, Simma; Schlessinger, Joseph

PATENT: PCT International ; WO 9826054 A2 DATE: 19980618
APPLICATION: WO 97US22565 (19971209) *US 32824 (19961211)
PAGES: 86 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: C12N-009/12A; C12N-015/12B; C12N-015/63B; C12N-001/21B; C12N-001/19B; C12N-005/10B
DESIGNATED COUNTRIES: AL; AM; AT; AU; AZ; BA; BB; BG; BR; BY; CA; CH; CN; CU; CZ; DE; DK; EE; ES; FI; GB; GE; GH; HU; ID; IL; IS; JP; KE; KG; KP; KR; KZ; LC; LK; LR; LS; LT; LU; LV; MD; MG; MK; MN; MW; MX; NO; NZ; PL; PT; RO; RU; SD; SE; SG; SI; SK; SL; TJ; TM; TR; TT; UA; UG; US; UZ; VN; YU; ZW; AM; AZ; BY; KG; KZ; MD; RU; TJ; TM DESIGNATED REGIONAL: GH; GM; KE; LS; MW; SD ; SZ; UG; ZW; AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
?

are in clinical trials or near clinical development by SUGEN, Zeneca, Novartis, Pfizer and Parke-Davis. A summary of the chemistry and activity of these agents is provided.

DRUG DESCRIPTORS:
*growth factor--drug development--dv; *growth factor--drug therapy--dt; * growth factor--pharmacology--pd; *protein tyrosine kinase inhibitor--drug development--dv; *protein tyrosine kinase inhibitor--drug therapy--dt; * protein tyrosine kinase inhibitor--pharmacology--pd; *protein tyrosine kinase--endogenous compound--ec; *quinazoline derivative--drug development --dv; *quinazoline derivative--drug therapy--dt; *quinazoline derivative --pharmacology--pd
adenosine triphosphate--endogenous compound--ec; phosphotyrosine --endogenous compound--ec; platelet derived growth factor--drug development --dv; platelet derived growth factor--drug therapy--dt; platelet derived growth factor--pharmacology--pd; vasculotropin--drug development--dv; vasculotropin--drug therapy--dt; vasculotropin--pharmacology--pd; epidermal growth factor receptor--endogenous compound--ec; isoxazole--drug development--dv; isoxazole--drug therapy--dt; isoxazole--pharmacology--pd; quinazoline--drug development--dv; quinazoline--drug therapy--dt; quinazoline--pharmacology--pd; pyrimidine derivative--drug development--dv; pyrimidine derivative--drug therapy--dt; pyrimidine derivative --pharmacology--pd; fibroblast growth factor receptor--drug development--dv ; fibroblast growth factor receptor--drug therapy--dt; fibroblast growth factor receptor--pharmacology--pd; unclassified drug
MEDICAL DESCRIPTORS:
*angiogenesis; *cancer--drug therapy--dt; *cancer--etiology--et; *fibrosis --drug therapy--dt; *fibrosis--etiology--et
oncogene; drug development; human; review
DRUG TERMS (UNCONTROLLED): indolinone derivative--drug development--dv; indolinone derivative--drug therapy--dt; indolinone derivative --pharmacology--pd
CAS REGISTRY NO.: 80449-02-1 (protein tyrosine kinase); 15237-44-2, 56-65-5 , 987-65-5 (adenosine triphosphate); 21820-51-9 (phosphotyrosine); 127464-60-2 (vasculotropin); 288-14-2 (isoxazole); 253-82-7 (quinazoline)
SECTION HEADINGS:
016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

22/9/18 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE

11690352 EMBASE No: 2002252994
Inhibition of constitutively active forms of mutant kit by multitargeted indolinone tyrosine kinase inhibitors
Liao A.T.; Chien M.B.; Shenoy N.; Mendel D.B.; McMahon G.; Cherrington J.M.; London C.A.
C.A. London, Department of Surgical Sciences, School of Veterinary Medicine, University of California, One Shields Ave, Davis, CA 95616 United States
AUTHOR EMAIL: calondon@ucdavis.edu
Blood (BLOOD) (United States) 15 JUL 2002, 100/2 (585-593)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal ; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 85

Mutations in the proto-oncogene c-kit, including point mutations, deletions, or duplications in the negative regulatory juxtamembrane (JM) domain or point mutations in the catalytic domain, have been observed in human and canine cancers and often result in constitutive activation of Kit in the absence of ligand binding. To identify a receptor tyrosine kinase (RTK) inhibitor capable of blocking the function of mutant Kit, we evaluated 3 indolinones (SU11652, SU11654, and SU11655) that act as competitive inhibitors of adenosine triphosphate binding to several members of the split kinase family of RTKs, including VEGFR, FGFR, PDGFR, and Kit. Mast cell lines expressing either wild type (WT) Kit, a point mutation in the JM domain, a tandem duplication in the JM domain, or a point mutation in the catalytic domain were used for these studies. All 3 indolinones inhibited phosphorylation of WT Kit in the presence of stem cell factor at concentrations as low as 0.01 muM. Autophosphorylation of both JM mutants was inhibited at 0.01 to 0.1 muM, resulting in cell cycle arrest within 24 hours, whereas autophosphorylation of the catalytic domain mutant was inhibited at 0.25 to 0.5 muM, resulting in cell death within 24 hours. poly(ADP-ribose) polymerase (PARP) cleavage was noted in all Kit mutant lines after indolinone treatment. In summary, SU11652, SU11654, and SU11655 are effective RTK inhibitors capable of disrupting the function of all forms of mutant Kit. Because the concentrations of drug necessary for receptor inhibition are readily achievable and nontoxic in vivo, these compounds may be useful in the treatment of spontaneous cancers expressing Kit mutations.

BRAND NAME/MANUFACTURER NAME: su 11652/Sugen; su 11654/Sugen; su 11655/Sugen
MANUFACTURER NAMES: Sugen
DRUG DESCRIPTORS:
*protein tyrosine kinase inhibitor--drug analysis--an; *protein tyrosine kinase inhibitor--pharmacology--pd; *stem cell factor; *protein tyrosine kinase
vasculotropin receptor; fibroblast growth factor receptor; platelet derived growth factor receptor; nicotinamide adenine dinucleotide adenosine diphosphate ribosyltransferase; unclassified drug
MEDICAL DESCRIPTORS:
*gene mutation
proto oncogene; point mutation; enzyme active site; ligand binding; autophosphorylation; cell cycle; cell death; drug receptor binding; drug inhibition; drug structure; nonhuman; controlled study; animal cell; article; priority journal
DRUG TERMS (UNCONTROLLED): 5 [(5 chloro 2 oxo 1,2 dihydro 3h indol 3 ylidene)methyl] n [2 (diethylamino)ethyl] 2,4 dimethyl 1h pyrrole 3 carboxamide--drug analysis--an; 5 [(5 chloro 2 oxo 1,2 dihydro 3h indol 3 ylidene)methyl] n [2 (diethylamino)ethyl] 2,4 dimethyl 1h pyrrole 3 carboxamide--pharmacology--pd; 5 [(5 fluoro 2 oxo 1,2 dihydro 3h indol 3 ylidene)methyl] 2,4 dimethyl n (2 pyrrolidin 1 ylethyl) 1h pyrrole 3 carboxamide--drug analysis--an; 5 [(5 fluoro 2 oxo 1,2 dihydro 3h indol 3 ylidene)methyl] 2,4 dimethyl n (2 pyrrolidin 1 ylethyl) 1h pyrrole 3 carboxamide--pharmacology--pd; 5 [(5 chloro 2 oxo 1,2 dihydro 3h indol 3 ylidene)methyl] 2,4 dimethyl n (2 pyrrolidin 1 ylethyl) 1h pyrrole 3 carboxamide--drug analysis--an; 5 [(5 chloro 2 oxo 1,2 dihydro 3h indol 3 ylidene)methyl] 2,4 dimethyl n (2 pyrrolidin 1 ylethyl) 1h pyrrole 3 carboxamide--pharmacology--pd; su 11652; su 11654; su 11655
CAS REGISTRY NO.: 80449-02-1 (protein tyrosine kinase); 301253-48-5 (vasculotropin receptor); 153424-51-2 (fibroblast growth factor receptor); 58319-92-9 (nicotinamide adenine dinucleotide adenosine diphosphate

ribosyltransferase)
SECTION HEADINGS:
016 Cancer
030 Clinical and Experimental Pharmacology
037 Drug Literature Index

22/9/21 (Item 21 from file: 73)
DIALOG(R)File 73:EMBASE

11232395 EMBASE No: 2001244891
Src inhibitors: Genomics to therapeutics
Sawyer T.; Boyce B.; Dalgarno D.; Iuliucci J.
T.K. Sawyer, ARIAD Pharmaceuticals, Cambridge, MA 02139 United States
Expert Opinion on Investigational Drugs (EXPERT OPIN. INVEST. DRUGS) (United Kingdom) 2001, 10/7 (1327-1344)
CODEN: EOIDE ISSN: 1354-3784
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 176

Following the milestone discoveries that identified Src as the first known protein tyrosine kinase and as a prototype oncogene, as well as Src transgenic studies to validate it as a promising therapeutic target for osteoporosis, intense efforts are being made to create Src inhibitor drugs. Drug discovery strategies focused on both the non-catalytic and catalytic domains of Src have successfully resulted in promising Src inhibitor lead compounds with potential therapeutic applications for osteoporosis, cancer, and other diseases. Some noteworthy examples of Src inhibitors are described, and their chemical diversity, structure-based design, and biological activities in vitro and in vivo are illustrated. The potency, selectivity, and in vivo efficacy of key Src inhibitors are being investigated in molecular, cellular and animal models. Consequently, Src inhibitor drug development is imminent, and current studies are well-poised to achieve the ultimate milestone of a Src inhibitor therapeutic.

BRAND NAME/MANUFACTURER NAME: ap 21773; ap 22526; ap 22408; nvp aak 980; cgp 76775; cgp 76030; pd 89828; pd 161570; pd 166285; pd 180970; rpr 108518 a; su 6656
DRUG DESCRIPTORS:
*protein tyrosine kinase inhibitor--drug analysis--an; *protein tyrosine kinase inhibitor--drug development--dv; *protein tyrosine kinase inhibitor --drug therapy--dt; *protein tyrosine kinase inhibitor--pharmacology--pd protein tyrosine kinase--endogenous compound--ec; purine derivative--drug analysis--an; purine derivative--drug development--dv; purine derivative --drug therapy--dt; purine derivative--pharmacology--pd; pyrazolopyrimidine derivative--drug analysis--an; pyrazolopyrimidine derivative--drug development--dv; pyrazolopyrimidine derivative--drug therapy--dt; pyrazolopyrimidine derivative--pharmacology--pd; pyrrolopyrimidine derivative--drug analysis--an; pyrrolopyrimidine derivative--drug development--dv; pyrrolopyrimidine derivative--drug therapy--dt; pyrrolopyrimidine derivative--pharmacology--pd; pyrimidine derivative--drug analysis--an; pyrimidine derivative--drug development--dv; pyrimidine derivative--drug therapy--dt; pyrimidine derivative--pharmacology--pd; pyrimidinone derivative--drug analysis--an; pyrimidinone derivative--drug development--dv; pyrimidinone derivative--drug therapy--dt; pyrimidinone derivative--pharmacology--pd; quinazoline derivative--drug analysis--an; quinazoline derivative--drug development--dv; quinazoline derivative--drug therapy--dt; quinazoline derivative--pharmacology--pd; quinoline derivative

--drug analysis--an; quinoline derivative--drug development--dv; quinoline derivative--drug therapy--dt; quinoline derivative--pharmacology--pd; indole derivative--drug analysis--an; indole derivative--drug development --dv; indole derivative--drug therapy--dt; indole derivative--pharmacology --pd; purvalanol B--drug analysis--an; purvalanol B--drug development--dv; purvalanol B--drug therapy--dt; purvalanol B--pharmacology--pd; 2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine--drug analysis--an; 2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine--drug development--dv; 2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine--drug therapy--dt; 2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine--pharmacology--pd; herbimycin A --drug analysis--an; herbimycin A--drug development--dv; herbimycin A--drug therapy--dt; herbimycin A--pharmacology--pd; staurosporine--drug analysis --an; staurosporine--drug development--dv; staurosporine--drug therapy--dt; staurosporine--pharmacology--pd; sulfate--drug analysis--an; sulfate--drug development--dv; sulfate--drug therapy--dt; sulfate--pharmacology--pd; unindexed drug; unclassified drug

MEDICAL DESCRIPTORS:

oncogene src; validation process; drug synthesis; osteoporosis--drug therapy--dt; drug research; catalysis; protein domain; cancer--drug therapy --dt; drug structure; drug design; drug activity; in vitro study; in vivo study; drug potency; drug selectivity; drug efficacy; molecular biology; cytology; nonhuman; animal experiment; animal model; review

DRUG TERMS (UNCONTROLLED): ap 21773--drug analysis--an; ap 21773--drug development--dv; ap 21773--drug therapy--dt; ap 21773--pharmacology--pd; ap 22526--drug analysis--an; ap 22526--drug development--dv; ap 22526--drug therapy--dt; ap 22526--pharmacology--pd; ap 22408--drug analysis--an; ap 22408--drug development--dv; ap 22408--drug therapy--dt; ap 22408 --pharmacology--pd; pyridopyrimidine derivative--drug analysis--an; pyridopyrimidine derivative--drug development--dv; pyridopyrimidine derivative--drug therapy--dt; pyridopyrimidine derivative--pharmacology--pd ; pyridopyrimidone derivative--drug analysis--an; pyridopyrimidone derivative--drug development--dv; pyridopyrimidone derivative--drug therapy --dt; pyridopyrimidone derivative--pharmacology--pd; indolinone--drug analysis--an; indolinone--drug development--dv; indolinone--drug therapy --dt; indolinone--pharmacology--pd; nvp aak 980--drug analysis--an; nvp aak 980--drug development--dv; nvp aak 980--drug therapy--dt; nvp aak 980 --pharmacology--pd; cgp 76775--drug analysis--an; cgp 76775--drug development--dv; cgp 76775--drug therapy--dt; cgp 76775--pharmacology--pd; cgp 76030--drug analysis--an; cgp 76030--drug development--dv; cgp 76030 --drug therapy--dt; cgp 76030--pharmacology--pd; pd 161570--drug analysis --an; pd 161570--drug development--dv; pd 161570--drug therapy--dt; pd 161570--pharmacology--pd; pd 166285--drug analysis--an; pd 166285--drug development--dv; pd 166285--drug therapy--dt; pd 166285--pharmacology--pd; pd 180970--drug analysis--an; pd 180970--drug development--dv; pd 180970 --drug therapy--dt; pd 180970--pharmacology--pd; rpr 108518 a--drug analysis--an; rpr 108518 a--drug development--dv; rpr 108518 a--drug therapy--dt; rpr 108518 a--pharmacology--pd; su 6656--drug analysis--an; su 6656--drug development--dv; su 6656--drug therapy--dt; su 6656 --pharmacology--pd; halistanol trisulfate--drug analysis--an; halistanol trisulfate--drug development--dv; halistanol trisulfate--drug therapy--dt; halistanol trisulfate--pharmacology--pd

CAS REGISTRY NO.: 80449-02-1 (protein tyrosine kinase); 212844-54-7 (purvalanol B); 179343-17-0 (2 amino 7 (3 tert butylureido) 6 (2,6 dichlorophenyl)pyrido[2,3 d]pyrimidine); 70563-58-5 (herbimycin A); 62996-74-1 (staurosporine); 14808-79-8 (sulfate)

SECTION HEADINGS:

016 Cancer
022 Human Genetics

033 Orthopedic Surgery
037 Drug Literature Index

22/9/25 (Item 25 from file: 73)
DIALOG(R)File 73:EMBASE

10557696 EMBASE No: 2000021293
Inhibition of transforming activity of the ret/ptc1 oncoprotein by a 2-indolinone derivative
Lanzi C.; Cassinelli G.; Pensa T.; Cassinis M.; Gambetta R.A.; Borrello M.G.; Menta E.; Pierotti M.A.; Zunino F.
C. Lanzi, Oncologia Sperimentale B, Istituto Nazionale Tumori, via Venezian 1, 20133 Milan Italy
AUTHOR EMAIL: Lanzi@istitutotumori.mi.it
International Journal of Cancer (INT. J. CANCER) (United States) 2000, 85/3 (384-390)
CODEN: IJCNA ISSN: 0020-7136
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 22

ret-derived oncogenes are frequently and specifically expressed in thyroid tumors. In contrast to the ret receptor, ret oncoproteins are characterized by ligand-independent tyrosine-kinase activity and tyrosine phosphorylation. In this study, novel synthetic arylidene 2-indolinone compounds were evaluated as inhibitors of the ret/ptc I tyrosine kinase. Four compounds inhibited ret/ptc1 activity in immunokinase assay (ICinf 5inf 0 27-42 muM) including one (1,3-dihydro-5,6-dimethoxy-3-[(4-hydroxyphenyl)methylene)- 2H-indol-2-one) (Cpd I) that selectively inhibited the anchorage-independent growth of NIH3T3 transformants expressing the ret/ptc1 gene (NIH3T3(Ptc1) cells). Following exposure to Cpd I, the transformed phenotype of NIH3T3(Ptc1) cells was reverted, within 24 hr, to a normal fibroblast-like morphology in adherent-cell culture. In these cells, the constitutive tyrosine phosphorylation of ret/ptc1, of the transducing adaptor protein shc and of a series of co-immunoprecipitated peptides became much reduced, as demonstrated by immunoprecipitation/Western-blot analyses. Data presented provide additional evidence that ret/ptc1 is directly implicated in malignant transformation, and demonstrate the ability of Cpd I to interfere in the signal transduction pathway constitutively activated by the ret/ptc1 oncoprotein. These results confirm the interest of the arylidene 2-indolinone class of tyrosine-kinase inhibitors as tools for the study of ret signaling and the control of cell proliferation in ret- and ret/ptcs-associated diseases.

DRUG DESCRIPTORS:
*oncoprotein; *protein tyrosine kinase; *indole derivative
MEDICAL DESCRIPTORS:
*enzyme inhibition; *cell proliferation
gene expression; protein phosphorylation; enzyme activity; malignant transformation; signal transduction; nonhuman; mouse; animal cell; article; priority journal
CAS REGISTRY NO.: 80449-02-1 (protein tyrosine kinase)
SECTION HEADINGS:
016 Cancer
? logoff hold
>>>KWIC option is not available in file(s): 399

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Set     Items   Description
S1       3335   E3-E50
S2         86   'FOCAL ADHESION KINASE 2'
S3     173883   'FOCAL ADHESION KINASE 2' OR DC='D4.680.265.60.680' OR R4:-
            R10
S4     176858   S1 OR S2 OR S3
S5      90232   S4 AND (INCREASE? OR DECREASE? OR REDUC? OR HIGHER? OR LOW-
            ER? OR INSUFFIC? OR DEPLET? OR DEFICIENT?)
S6      32420   S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR
             CROHN? OR COLITIS?)
S7       4690   S5 AND (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAMMAT? OR
             CROHN? OR COLITIS?)/TI
S8         43   S4/TI (100N) (DISEASE? OR CANCER? OR AUTOIMMUNE? OR INFLAM-
            MAT? OR CROHN? OR COLITIS?)
S9       2437   S4 AND ((CONNECTIVE? (3N) TISSUE?) OR ARTHRIT? OR DEGENERA-
            TIV?)
S10        43   S8
S11        16   RD (unique items)
S12       182   S4 AND ARTHRIT?/TI
S13        28   S4 AND COLITIS?/TI
S14        25   S4 AND CROHN?/TI
S15   6175059   REVIEW? OR TUTOR?
S16     17720   S15 AND S4
S17        12   S4/TI AND (DISEASE? OR COLLAGEN? OR ARTHRITIS? OR COLITIS?
            OR CROHN? OR INFLAMMAT?)/TI
S18       108   S4 (5N) LEVEL?
S19        71   S18 (25N)(INCREASE? OR DECREASE? OR HIGHER? OR LOWER? OR I-
            MBALANCE? OR DIMINISH? OR REDUC?)
S20        25   RD (unique items)
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 20/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2005 Dialog. All rts. reserv.

18254448   PMID: 16039993
  Role of PYK2 in the development of obesity and insulin resistance.
  Yu  Ying; Ross Stuart A; Halseth Amy E; Hollenbach Paul W; Hill Ronald J;
Gulve Eric A; Bond Brian R
  PFIZER  Global Research and Development, Cardiovascular Pharmacology, 700
Chesterfield Parkway West, Chesterfield, MO 63017, USA.
  Biochemical and biophysical research communications (United States)   Sep
9 2005,  334  (4)  p1085-91,  ISSN 0006-291X   Journal Code: 0372516
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: In Data Review
  Subfile:   INDEX MEDICUS
  Non-receptor proline-rich tyrosine kinase-2 (PYK2), which is activated by
phosphorylation  of  one  or  more  of  its  tyrosine  residues,  has  been
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implicated in the regulation of GLUT4 glucose transporter translocation and glucose transport. Some data favor a positive role of PYK2 in stimulating glucose transport, whereas other studies suggest that PYK2 may participate in the induction of insulin resistance. To ascertain the importance of PYK2 in the setting of obesity and insulin resistance, we (1) evaluated the regulation of PYK2 in mice fed a high-fat diet and (2) characterized body and glucose homeostasis in wild type (WT) and PYK2((-/-)) mice on different diets. We found that both PYK2 expression and phosphorylation were significantly increased in liver and adipose tissues harvested from high-fat diet fed mice. Wild type and PYK2((-/-)) mice were fed a high-fat diet for 8 weeks to induce insulin resistance/obesity. Surprisingly, in response to this diet PYK2((-/-)) mice gained significantly more weight than WT mice (18.7+/-1.2g vs. 9.5+/-0.6g). Fasting serum leptin and insulin and blood glucose levels were significantly increased in high-fat diet fed mice irrespective of the presence of PYK2 protein. There was a close correlation between serum leptin and body weight. Intraperitoneal glucose tolerance tests revealed that as expected, the high-fat diet resulted in **increased** blood glucose levels following glucose administration in wild type mice compared to those fed normal chow. An even greater **increase** in blood glucose **levels** was observed in **PYK2** ((-/-)) mice compared to wild type mice. These results demonstrate that a lack of PYK2 exacerbates weight gain and development of glucose intolerance/insulin resistance induced by a high-fat diet, suggesting that PYK2 may play a role in slowing the development of obesity, insulin resistance, and/or frank diabetes.

Record Date Created: 20050801

20/9/2 (Item 2 from file: 155)

18218071 PMID: 15829561

PYK2 regulates SERCA2 gene expression in neonatal rat ventricular myocytes.

Heidkamp Maria C; Scully Brian T; Vijayan Kalpana; Engman Steven J; Szotek Erika L; Samarel Allen M

The Cardiovascular Institute, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois, USA.

American journal of physiology. Cell physiology (United States) Aug 2005, 289 (2) pC471-82, ISSN 0363-6143 Journal Code: 100901225

Contract/Grant No.: HL-68476; HL; NHLBI; R01-HL-34328; HL; NHLBI; R01-HL-63711; HL; NHLBI

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

Subfile: INDEX MEDICUS

The nonreceptor protein tyrosine kinase (PTK) proline-rich tyrosine kinase 2 (PYK2) has been implicated in cell signaling pathways involved in left ventricular hypertrophy and heart failure, but its exact role has not been elucidated. In this study, replication-defective adenoviruses (Adv) encoding green fluorescent protein (GFP)-tagged, wild-type (WT), and mutant forms of PYK2 were used to determine whether PYK2 overexpression activates MAPKs, and downregulates SERCA2 mRNA levels in neonatal rat ventricular myocytes (NRVM). PYK2 overexpression significantly decreased SERCA2 mRNA (as determined by Northern blot analysis and real-time RT-PCR) to 54 +/- 4% of Adv-GFP-infected cells 48 h after Adv infection. Adv-encoding kinase-deficient (KD) and Y(402)F phosphorylation-deficient mutants of PYK2

also significantly **reduced** SERCA2 mRNA (WT>KD>Y(402)F). Conversely, the PTK inhibitor PP2 (which blocks PYK2 phosphorylation by Src-family PTKs) significantly **increased** SERCA2 mRNA **levels** . **PYK2** overexpression had no effect on ERK1/2, but **increased** JNK1/2 and p38(MAPK) phosphorylation from fourfold to eightfold compared with GFP overexpression. Activation of both "stress-activated" protein kinase cascades appeared necessary to reduce SERCA2 mRNA levels. Adv-mediated overexpression of constitutively active (ca)MKK6 or caMKK7, which activated only p38(MAPK) or JNKs, respectively, was not sufficient, whereas combined infection with both Adv reduced SERCA2 mRNA levels to 45 +/- 12% of control. WTPYK2 overexpression also significantly reduced SERCA2 promoter activity, as determined by transient transfection of a 3.8-kb SERCA2 promoter-luciferase construct. Thus a PYK2-dependent signaling cascade may have a role in abnormal cardiac Ca(2+) handling in left ventricular hypertrophy and heart failure via downregulation of SERCA2 gene transcription.

Record Date Created: 20050708

Date of Electronic Publication: 20050413

20/9/3 (Item 3 from file: 155)

18168648 PMID: 15970382

Suppression of postsynaptic density protein 95 by antisense oligonucleotides diminishes postischemic pyramidal cell death in rat hippocampal CA1 subfield.

Hou Xiao-Yu; Zhang Guang-Yi; Wang De-Guang; Guan Qiu-Hua; Yan Jing-Zhi

Research Center for Biochemistry and Molecular Biology, Xuzhou Medical College, University of Science & Technology of China, 84 West Huai-hai Road, Xuzhou, Jiangsu 221002, PR China.

Neuroscience letters (Ireland) Sep 16 2005, 385 (3) p230-3, ISSN 0304-3940 Journal Code: 7600130

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Data Review

Subfile: INDEX MEDICUS

Our previous investigation has shown that postsynaptic density protein 95 (PSD-95) is critical for the Src family kinases-mediated tyrosine phosphorylation of N-methyl-d-aspartate receptor subunit 2A (NR2A) in the postischemic hippocampus. To clarify the roles of PSD-95 in the ischemic brain damage, histological method was performed to examine the effects of PSD-95 antisense oligonucleotides (AS) on the postischemic delayed cell death in rat hippocampus. Transient (15min) brain ischemia was induced by the four-vessel occlusion method in Sprague-Dawley rats. Five days of reperfusion following brain ischemia (I/R5d) led to hippocampal CA1 pyramidal cell death upward of 90%. Intracerebroventricular infusion of AS (every 24h for 3 days before ischemia) not only decreased the PSD-95 expression but also increased the number of surviving pyramidal neurons, while missense oligonucleotides (MS) had no effects. To further investigate the mechanisms underlying the neuroprotection of PSD-95 deficiency, the interaction of proline-rich tyrosine kinase 2 (Pyk2) with NR2A as well as autophosphorylation (Tyr402) of Pyk2 were detected. Immunoprecipitation and immunoblot analysis showed that preischemic treatment with AS, but not MS or vehicle, attenuated the I/R6h-induced **increases** in Pyk2-NR2A association and **Pyk2** autophosphorylation. The protein **levels** of NR2A and **Pyk2** had no differences under the above conditions. Our data suggest

that the recruitments of ion channels and signaling molecules may be involved in the PSD-95 neurotoxicity in the postischemic hippocampus.
Record Date Created: 20050718

20/9/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

15196871 PMID: 14676843
Vascular endothelial growth factor-mediated activation of p38 is dependent upon Src and RAFTK/Pyk2.
McMullen Meghan; Keller Rebecca; Sussman Mark; Pumiglia Kevin
Center for Cell Biology and Cancer Research, Albany Medical College, Albany NY, USA.
Oncogene (England) Feb 12 2004, 23 (6) p1275-82, ISSN 0950-9232 Journal Code: 8711562
Contract/Grant No.: R01-CA-81419; CA; NCI; T32-HL-07194; HL; NHLBI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Vascular endothelial growth factor (VEGF) induces activation of p38 mitogen-activated protein kinase (MAPK) in primary endothelial cells and may be critical for VEGF-induced angiogenesis. We investigated the molecular basis for p38 activation in response to VEGF. The expression of a C-terminal splice variant of FAK, FRNK, had no affect on VEGF-induced activation of p38; however, expression of a dominant-negative RAFTK/Pyk2 mutant led to a decrease in the activation of p38, but had no affect on extracellular signal-regulated kinase (ERK). Since calcium regulates RAFTK/Pyk2, we investigated its role in p38 activity. Preincubation with EGTA suppressed p38 activation, while calcium ionophore induced p38 activity. Inhibition of phospholipase C (PLC) resulted in complete inhibition of ERK, while having no affect on p38 activity. These data suggested a bifurcation in the regulation of MAPKs that occurs at the **level** of PLC and RAFTK/ **Pyk2** activation. Src family kinases interact with RAFTK/Pyk2. Inhibition of Src by either pharmacological or genetic means **decreased** p38 activity. Finally, we found that both Src and RAFTK/Pyk2 were essential for endothelial cell migration. These data identified a novel regulatory network involving extracellular calcium, RAFTK/Pyk2, Src and p38. This signaling network appears to be critical for VEGF-induced endothelial cell migration.
Tags: Research Support, U.S. Gov't, P.H.S.
Descriptors: *Chemotaxis--physiology--PH; *Endothelium, Vascular --physiology--PH; *Mitogen-Activated Protein Kinases--metabolism--ME; *Protein-Tyrosine Kinase--metabolism--ME; *Vascular Endothelial Growth Factor A--pharmacology--PD; *src-Family Kinases--metabolism--ME; Calcium --physiology--PH; Cells, Cultured; Chemotaxis--drug effects--DE; Culture Media, Serum-Free; Egtazic Acid--pharmacology--PD; Endothelium, Vascular --drug effects--DE; Enzyme Activation; Humans; Neovascularization, Physiologic; Umbilical Veins; p38 Mitogen-Activated Protein Kinases
CAS Registry No.: 0 (Culture Media, Serum-Free); 0 (Vascular Endothelial Growth Factor A); 67-42-5 (Egtazic Acid); 7440-70-2 (Calcium)
Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.112 (src-Family Kinases); EC 2.7.1.37 (Mitogen-Activated Protein Kinases); EC 2.7.1.37 (p38

Mitogen-Activated Protein Kinases)
Record Date Created: 20040212
Record Date Completed: 20040309

20/9/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14947670 PMID: 12946883

Antidepressant effect of the calcium-activated tyrosine kinase Pyk2 in the lateral septum.

Sheehan Teige P; Neve Rachael L; Duman Ronald S; Russell David S
Department of Psychiatry, Division of Molecular Psychiatry, Yale University School of Medicine, Connecticut Mental Health Center, New Haven, Connecticut 06508, USA.

Biological psychiatry (United States) Sep 1 2003, 54 (5) p540-51, ISSN 0006-3223 Journal Code: 0213264
Contract/Grant No.: DA 00302; DA; NIDA
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Accumulating evidence indicates that neural activity in the lateral septum (LS) influences the pathophysiology of depression and therapeutic effectiveness of antidepressant drugs. For example, the development of behavioral deficits in animal screens for antidepressant drug activity corresponds with a blunting of LS activity, whereas chronic treatment with antidepressants enhances cell firing in the LS; however, the molecular mechanisms underlying such behavioral functions of the LS have not been determined. The nonreceptor tyrosine kinase Pyk2 is highly expressed in the LS and plays important roles in regulating cellular excitability and synaptic plasticity, making it an attractive candidate for regulating the effects of stress and antidepressants on LS functioning and behavior. We provide evidence that stress decreases Pyk2 phosphorylation in the LS, whereas enhancing Pyk2 expression in LS neurons has an antidepressant effect behaviorally.Pyk2 messenger ribonucleic acid (mRNA) expression in the rat forebrain was detected by in situ hybridization, and a brief description of the distribution of Pyk2 mRNA in selected areas is presented. Levels of total Pyk2 protein and phosphorylated Pyk2 were subsequently measured in the LS and hippocampus following stress exposure, as were levels of extracellular stimuli-regulated kinase (Erk) and phospho-Erk. Herpes simplex virus (HSV)-mediated gene transfer was then used to enhance Pyk2 expression in the LS, and the effect this had on behavior in the learned helplessness model of depression was evaluated.High **levels** of **Pyk2** mRNA were detected in a number of forebrain regions, including the hippocampus and LS. Following acute stress exposure, subjects showed a **decrease** in phosphorylated Pyk2 and Erk in the LS but not in the hippocampus. Total **levels** of **Pyk2** and Erk remained unchanged following stress. In the learned helplessness paradigm, injection of HSV-Pyk2 into the LS prevented the active avoidance deficit caused by exposure to inescapable shock, indicative of an antidepressant effect.These results indicate that following acute stress, Pyk2 and Erk activity in the LS are decreased, whereas experimentally increasing Pyk2 activity in LS neurons reverses the behavioral deficits of acute, inescapable stress. These findings establish a role for the tyrosine kinase Pyk2 in the biochemical and behavioral responses to stress and suggest a possible role in the

pathophysiology of depression, particularly notable considering Pyk2's role in promoting synaptic plasticity.
Tags: Comparative Study; Male; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.
Descriptors: *Protein-Tyrosine Kinase--metabolism--ME; *Septum of Brain --metabolism--ME; *Stress--metabolism--ME; Animals; Depressive Disorder --enzymology--EN; Depressive Disorder--metabolism--ME; Gene Expression Regulation; Gene Transfer Techniques; Helplessness, Learned; Immunoblotting ; In Situ Hybridization; Neurons--enzymology--EN; Neurons--metabolism--ME; Phosphorylation; Protein-Tyrosine Kinase--genetics--GE; RNA, Messenger --metabolism--ME; Rats; Rats, Sprague-Dawley; Septum of Brain--enzymology --EN; Simplexvirus--genetics--GE; Stress--psychology--PX
CAS Registry No.: 0 (RNA, Messenger)
Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase)
Record Date Created: 20030829
Record Date Completed: 20031107

20/9/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14491566 PMID: 12228222
Activation of pyk2/related focal adhesion tyrosine kinase and focal adhesion kinase in cardiac remodeling.
Melendez Jaime; Welch Sara; Schaefer Erik; Moravec Christine S; Avraham Shalom; Avraham Hava; Sussman Mark A
Children's Hospital Research Foundation, Division of Molecular Cardiovascular Biology, Cincinnati, Ohio 45229, USA.
Journal of biological chemistry (United States) Nov 22 2002, 277 (47) p45203-10, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: HL58224; HL; NHLBI; HL66035; HL; NHLBI; HL67245; HL; NHLBI
Publishing Model Print-Electronic
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Cellular remodeling during progression of dilation involves focal adhesion contact reorganization. However, the signaling mechanisms and structural consequences leading to impaired cardiomyocyte adhesion are poorly defined. These events were studied in tropomodulin-overexpressing transgenic mice that develop dilated cardiomyopathy associated with chronic elevation of intracellular calcium. Analysis of tropomodulin-overexpressing transgenic hearts by immunoblot and confocal microscopy revealed activation and redistribution of signaling molecules known to regulate adhesion. Calcium-dependent pyk2/related focal adhesion tyrosine kinase (RAFTK) showed changes in expression and phosphorylation state, similar to changes observed for a related downstream target molecule of pyk2/RAFTK termed focal adhesion kinase. Paxillin, the target substrate molecule for focal adhesion kinase phosphorylation, was redistributed in tropomodulin-overexpressing transgenic hearts with enhanced paxillin phosphorylation and cleavage. Certain aspects of the in vivo signaling phenotype including **increased** paxillin phosphorylation could be recapitulated in vitro using neonatal rat cardiomyocytes infected with recombinant adenovirus to overexpress tropomodulin. In addition, increasing intracellular calcium **levels** with ionomycin induced **pyk2** /RAFTK

phosphorylation, and adenovirally mediated expression of wild-type pyk2/RAFTK resulted in **increased** phospho- **pyk2** /RAFTK **levels** and concomitant paxillin phosphorylation. Collectively, these results delineate a cardiomyocyte signaling pathway associated with dilation that has potential relevance for cardiac remodeling, focal adhesion reorganization, and loss of contractility.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Heart--physiology--PH; *Protein-Tyrosine Kinase--metabolism --ME; *Ventricular Remodeling; Animals; Animals, Newborn; Calcium --metabolism--ME; Carrier Proteins--genetics--GE; Carrier Proteins --metabolism--ME; Cell Adhesion--physiology--PH; Cells, Cultured; Cytoskeletal Proteins--metabolism--ME; Cytoskeleton--metabolism--ME; Enzyme Activation; Focal Adhesions--metabolism--ME; Immunohistochemistry; Mice; Mice, Transgenic; Microfilament Proteins--genetics--GE; Microfilament Proteins--metabolism--ME; Myocytes, Cardiac--cytology--CY; Myocytes, Cardiac--metabolism--ME; Phosphoproteins--metabolism--ME; Phosphorylation; Protein Transport--physiology--PH; Rats; Rats, Sprague-Dawley; Signal Transduction--physiology--PH

CAS Registry No.: 0 (Carrier Proteins); 0 (Cytoskeletal Proteins); 0 (Microfilament Proteins); 0 (Phosphoproteins); 0 (paxillin); 146409-61-2 (tropomodulin); 7440-70-2 (Calcium)

Enzyme No.: EC 2.7.1.- (focal adhesion protein-tyrosine kinase); EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase)

Record Date Created: 20021118

Record Date Completed: 20030107

Date of Electronic Publication: 20020912

20/9/7 (Item 7 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14438138 PMID: 12376862

[Expression analysis of protein tyrosine kinases of the FAK (focal adhesion kinase) family in osteosarcoma]

Untersuchungen zur Expression von Proteintyrosinkinasen der FAK- (Focal Adhesion Kinase-)Familie in Osteosarkomen.

Schroder A; Delling G; Kaiser E A

Abteilung Osteopathologie/Zentrum fur Biomechanik, Pathologisches Institut, Universitatskrankenhaus Hamburg-Eppendorf, Hamburg, Germany.

Der Pathologe (Germany) Sep 2002, 23 (5) p361-6, ISSN 0172-8113 Journal Code: 8006541

Publishing Model Print-Electronic

Document type: Journal Article ; English Abstract

Languages: GERMAN

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

AIMS: Expression analysis of the protein tyrosine kinases, focal adhesion kinase (FAK) and proline-rich tyrosine kinase2 (Pyk2) in high grade osteosarcomas. MATERIALS AND METHODS: Expression of the kinases was evaluated qualitatively by immunohistochemical staining and quantitatively by real-time PCR. RESULTS: Osteoblastic cells of high grade osteosarcomas show a distinct FAK expression but an overexpression at the transcriptional **level** could not be detected. The **Pyk2** -mRNA expression was **decreased** in osteosarcomas. CONCLUSION: An altered relationship of FAK and Pyk2 was observed for different tumors and could also be important for osteosarcoma

development.
Tags: Female; Male
Descriptors: *Bone Neoplasms--enzymology--EN; *Osteosarcoma--enzymology --EN; *Protein-Tyrosine Kinase--genetics--GE; Adolescent; Adult; Aged; Bone Neoplasms--genetics--GE; Bone Neoplasms--pathology--PA; Child; Child, Preschool; Humans; Immunohistochemistry; Middle Aged; Osteosarcoma --genetics--GE; Osteosarcoma--pathology--PA; Polymerase Chain Reaction --methods--MT
Enzyme No.: EC 2.7.1.- (focal adhesion protein-tyrosine kinase); EC 2.7.1.112 (Protein-Tyrosine Kinase)
Record Date Created: 20021011
Record Date Completed: 20021223
Date of Electronic Publication: 20020814

20/9/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14309718 PMID: 12124218
PYK2 expression and phosphorylation increases in pressure overload-induced left ventricular hypertrophy.
Bayer Allison L; Heidkamp Maria C; Patel Nehu; Porter Michael J; Engman Steven J; Samarel Allen M
The Cardiovascular Institute and Department of Physiology, Stritch School of Medicine, Loyola University Chicago, 2160 First Avenue, Maywood, IL 60153, USA.
American journal of physiology. Heart and circulatory physiology (United States) Aug 2002, 283 (2) pH695-706, ISSN 0363-6135 Journal Code: 100901228
Contract/Grant No.: F32 HL 10313; HL; NHLBI; F32 HL 68476; HL; NHLBI; HL 34328; HL; NHLBI; HL 63711; HL; NHLBI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS
Proline-rich tyrosine kinase 2 (PYK2) is a member of the focal adhesion kinase (FAK) family of nonreceptor protein tyrosine kinases. PYK2 has been implicated in linking G protein-coupled receptors to activation of mitogen-activated protein kinase cascades and cellular growth in a variety of cell types. To determine whether PYK2 expression and phosphorylation is altered in left ventricular (LV) myocardium undergoing LV hypertrophy (LVH) and heart failure in vivo, suprarenal abdominal aortic coarctation was performed in 160-g male Sprague-Dawley rats. Immunohistochemistry and Western blotting were performed on LV tissue 1, 8, and 24 wk after aortic banding. Aortic banding produced sustained hypertension and gradually developing LVH. **PYK2 levels** were **increased** 1.8 +/- 0.2-, 2.7 +/- 0.6-, and 2.0 +/- 0.2-fold in 1-, 8-, and 24-wk banded animals compared with their respective sham-operated controls. The increase in PYK2 expression was paralleled by an increase in PYK2 phosphorylation, both of which preceded the development of LVH. Immunohistochemistry revealed that enhanced PYK2 expression occurred predominantly in the cardiomyocyte population. Furthermore, there was a high degree of correlation ($R = 0.75$; $P < 0.001$) between the **level** of **PYK2** and the degree of LVH in 24-wk sham and banded animals. In contrast, FAK levels and FAK phosphorylation were not **increased** before the development of LVH. However, there was a high degree of correlation ($R = 0.68$; $P < 0.001$) between the level of FAK

and the degree of LVH in 24-wk sham and banded rats. There was also a significant increase in the ratio of phosphospecific anti-FAK to FAK at this time point. These data are consistent with a role for PYK2 in the induction of pressure overload-induced cardiomyocyte hypertrophy, and suggest that PYK2 and FAK have distinctly different roles in LVH progression.

Tags: Male; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Hypertension--complications--CO; *Hypertrophy, Left Ventricular--enzymology--EN; *Hypertrophy, Left Ventricular--etiology--ET; *Protein-Tyrosine Kinase--metabolism--ME; Adaptation, Physiological; Animals; Cardiac Output, Low--enzymology--EN; Disease Progression; Heart Ventricles; Hypertrophy, Left Ventricular--pathology--PA; Myocardium --enzymology--EN; Myocardium--pathology--PA; Phosphorylation; Rats; Rats, Sprague-Dawley; Tissue Distribution; Tyrosine--metabolism--ME

CAS Registry No.: 55520-40-6 (Tyrosine)

Enzyme No.: EC 2.7.1.- (focal adhesion protein-tyrosine kinase); EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase)

Record Date Created: 20020718

Record Date Completed: 20020815

20/9/9 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14297722 PMID: 12111044

Angiotensin II-augmented migration of VSMCs towards PDGF-BB involves Pyk2 and ERK 1/2 activation.

Blaschke Florian; Stawowy Philipp; Kappert Kai; Goetze Stephan; Kintscher Ulrich; Wollert-Wulf Brigitte; Fleck Eckart; Graf Kristof

Deutsches Herzzentrum Berlin, Department of Medicine/Cardiology, Augustenburger Platz 1, 13353 Berlin, Germany.

Basic research in cardiology (Germany) Jul 2002, 97 (4) p334-42, ISSN 0300-8428 Journal Code: 0360342

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Activation of the local and systemic renin-angiotensin system is directly and indirectly involved in mechanisms of vascular remodeling during chronic hypertension. This study investigated the effect of angiotensin II (AII) on rat vascular smooth muscle cell (VSMC) migration towards platelet-derived growth factor-BB (PDGF-BB) in vitro. Pre-treatment with AII (1 microM) for 48 or 72 h induced a significant increase in PDGF-BB-directed migration by 77 +/- 21 % and 58 +/- 24 %, respectively (both $p < 0.01$). This effect was concentration dependent and inhibited by the selective angiotensin receptor type I (AT(1)) blocker DUP 753. PDGF-directed migration of VSMCs was significantly inhibited by antibodies against beta(3)-and beta(5)-integrins, indicating an important role of these integrins in VSMC migration. However, AII augmented migration was not accompanied by an increased expression of beta(3)- and beta(5)-integrin mRNA and protein levels in VSMCs. Inhibition of the mitogen-activated protein kinase ERK 1/2 with PD 98059 (30 microM) completely abolished the effect of AII on PDGF-BB-directed VSMC migration ($p < 0.01$). The proline-rich tyrosine kinase 2 (Pyk2) and focal adhesion kinase (FAK) are cytoskeleton-associated

protein kinases participating in integrin-dependent signaling. Therefore, expression and phosphorylation of these kinases was determined 48 h after AII treatment, revealing a significant **increase** in **Pyk2** and FAK protein **levels** (up to 2-fold, both $p < 0.05$) and **increased** phosphorylation of Pyk2 (2-fold, $p < 0.05$) and ERK 1/2 (4-fold, $p < 0.05$) as compared to controls. Furthermore, immunofluorescence and Western blot analysis demonstrated a translocation of Pyk2 from the plasma membrane to the cytosol, as well as a perinuclear enrichment of ERK 1/2 protein 48 h after AII treatment. In conclusion, our data suggest that changes in the levels of Pyk2 and ERK 1/2 phosphorylation, responsible for integrin-dependent signaling, as well as their subcellular translocation are important for the enhanced chemotactic response of VSMCs after AII pre-treatment.

Tags: Research Support, Non-U.S. Gov't

Descriptors: *Angiotensin II--pharmacology--PD; *Cell Movement --drug effects--DE; *MAP Kinase Signaling System--drug effects--DE; *Muscle, Smooth, Vascular--cytology--CY; *Protein-Tyrosine Kinase--metabolism--ME; *Vasoconstrictor Agents--pharmacology--PD; Angiogenesis Inducing Agents --pharmacology--PD; Animals; Cells, Cultured; Flow Cytometry; Integrins --metabolism--ME; Mitogen-Activated Protein Kinase 1--metabolism--ME; Mitogen-Activated Protein Kinase 3; Mitogen-Activated Protein Kinases --metabolism--ME; Muscle, Smooth, Vascular--metabolism--ME; Phosphorylation ; Platelet-Derived Growth Factor--pharmacology--PD; Rats; Rats, Sprague-Dawley

CAS Registry No.: 0 (Angiogenesis Inducing Agents); 0 (Integrins); 0 (MAP Kinase Signaling System); 0 (Platelet-Derived Growth Factor); 0 (Vasoconstrictor Agents); 0 (platelet-derived growth factor BB); 11128-99-7 (Angiotensin II)

Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.37 (Mitogen-Activated Protein Kinase 1); EC 2.7.1.37 (Mitogen-Activated Protein Kinase 3); EC 2.7.1.37 (Mitogen-Activated Protein Kinases)

Record Date Created: 20020711

Record Date Completed: 20030207

20/9/10 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14288216 PMID: 12097497

Metabotropic glutamate receptor 1-induced upregulation of NMDA receptor current: mediation through the Pyk2/Src-family kinase pathway in cortical neurons.

Heidinger Valerie; Manzerra Pat; Wang Xue Qing; Strasser Uta; Yu Shan-Ping; Choi Dennis W; Behrens M Margarita

Department of Neurology and Center for the Study of the Nervous System Injury, Washington University School of Medicine, St. Louis, Missouri 63110, USA.

Journal of neuroscience - the official journal of the Society for Neuroscience (United States) Jul 1 2002, 22 (13) p5452-61, ISSN 1529-2401 Journal Code: 8102140

Contract/Grant No.: NS 30337; NS; NINDS

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

The mechanism underlying the upregulation of NMDA receptor function by

group I metabotropic glutamate receptors (mGluRs), including mGluR1 and 5, is not known. Here we show that in cortical neurons, brief selective activation of group I mGluRs with (S)-3,5-dihydroxy-phenylglycine (DHPG) induced a Ca(2+)-calmodulin-dependent activation of Pyk2/CAKbeta and the Src-family kinases Src and Fyn that was independent of protein kinase C (PKC). Activation of Pyk2 and Src/Fyn kinases led to increased tyrosine phosphorylation of NMDA receptor subunits 2A and B (NR2A/B) and was blocked by a selective mGluR1 antagonist, 7-(hydroxyamino)cyclopropa[b]chromen-1a-carboxylate ethyl ester, but not an mGluR5 antagonist, 2-methyl-6-(phenylethynyl)pyridine. Functional linkage between mGluR1 activation and NR2A tyrosine phosphorylation through Pyk2 and Src was also demonstrated after expression of these elements in human embryonic kidney 293 cells. Supporting functional consequences, selective activation of mGluR1 by DHPG induced a potentiation of NMDA receptor-mediated currents that was blocked by inhibiting mGluR1 or Src-family kinases. Furthermore, antagonizing calmodulin or mGluR1, but not PKC, **reduced** the basal tyrosine phosphorylation **levels** of **Pyk2** and Src, suggesting that mGluR1 may control the basal activity of these kinases and thus the tyrosine phosphorylation levels of NMDA receptors.

Tags: Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, Non-P.H.S.; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Cerebral Cortex--physiology--PH; *Protein-Tyrosine Kinase --metabolism--ME; *Receptors, Metabotropic Glutamate--metabolism--ME; *Receptors, N-Methyl-D-Aspartate--physiology--PH; *src-Family Kinases --metabolism--ME; Animals; Cell Line; Cells, Cultured; Cerebral Cortex --cytology--CY; Cerebral Cortex--enzymology--EN; Electric Conductivity; Excitatory Amino Acid Agonists--pharmacology--PD; Glycine --analogs and derivatives--AA; Glycine--pharmacology--PD; Humans; Mice; Neurons--drug effects--DE; Neurons--enzymology--EN; Neurons--physiology--PH; Phosphorylation; Proto-Oncogene Protein pp60(c-src)--metabolism--ME; Proto-Oncogene Proteins--metabolism--ME; Receptors, Metabotropic Glutamate--physiology--PH; Receptors, N-Methyl-D-Aspartate--metabolism--ME; Resorcinols --pharmacology--PD; Signal Transduction; Up-Regulation

CAS Registry No.: 0 (Excitatory Amino Acid Agonists); 0 (NR2A NMDA receptor); 0 (NR2B NMDA receptor); 0 (Proto-Oncogene Proteins); 0 (Receptors, Metabotropic Glutamate); 0 (Receptors, N-Methyl-D-Aspartate); 0 (Resorcinols); 0 (metabotropic glutamate receptor 5); 0 (metabotropic glutamate receptor type 1); 0 (proto-oncogene protein c-fyn); 146255-66-5 (3,5-dihydroxyphenylglycine); 56-40-6 (Glycine)

Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.112 (Proto-Oncogene Protein pp60(c-src)); EC 2.7.1.112 (src-Family Kinases)

Record Date Created: 20020704

Record Date Completed: 20020729

20/9/11 (Item 11 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13778031 PMID: 11441106

Glucocorticoid augmentation of macrophage capacity for phagocytosis of apoptotic cells is associated with reduced **p130Cas expression, loss of paxillin/** pyk2 **phosphorylation, and high** levels **of active Rac.**

Giles K M; Ross K; Rossi A G; Hotchin N A; Haslett C; Dransfield I

Medical Research Council Centre for Inflammation Research, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG, United Kingdom.

Journal of immunology (Baltimore, Md. - 1950) (United States) Jul 15 2001, 167 (2) p976-86, ISSN 0022-1767 Journal Code: 2985117R

Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: AIM; INDEX MEDICUS

Phagocytic clearance of apoptotic granulocytes has a pivotal role in determining an inflammatory outcome, resolution or progression to a chronic state associated with development of fibrotic repair mechanisms, and/or autoimmune responses. In this study, we describe reprogramming of monocyte to macrophage differentiation by glucocorticoids, resulting in a marked augmentation of their capacity for phagocytosis of apoptotic neutrophils. This monocyte/macrophage phenotype was characterized by decreased phosphorylation, and therefore recruitment of paxillin and pyk2 to focal contacts and a down-regulation of p130Cas, a key adaptor molecule in integrin adhesion signaling. Glucocorticoid-treated cells also displayed higher levels of active Rac and cytoskeletal activity, which were mirrored by increases in phagocytic capability for apoptotic neutrophils. We propose that changes in the capacity for reorganization of cytoskeletal elements induced by glucocorticoids are essential for efficient phagocytic uptake of apoptotic cells.

Tags: Research Support, Non-U.S. Gov't

Descriptors: *Adjuvants, Immunologic--pharmacology--PD; *Apoptosis--drug effects--DE; *Cytoskeletal Proteins--metabolism--ME; *Dexamethasone --pharmacology--PD; *Macrophages--drug effects--DE; *Phagocytosis --drug effects--DE; *Phosphoproteins--biosynthesis--BI; *Phosphoproteins --metabolism--ME; *Protein-Serine-Threonine Kinases--metabolism--ME; *Protein-Tyrosine Kinase--metabolism--ME; *Proteins; Apoptosis--immunology --IM; Cells, Cultured; Cytoskeletal Proteins--antagonists and inhibitors --AI; Cytoskeleton--drug effects--DE; Cytoskeleton--metabolism--ME; Humans ; Immunophenotyping; Macrophages--immunology--IM; Macrophages--metabolism --ME; Neutrophils--cytology--CY; Neutrophils--immunology--IM; Phosphoprote ins--antagonists and inhibitors--AI; Protein-Serine-Threonine Kinases --biosynthesis--BI; Protein-Tyrosine Kinase--antagonists and inhibitors--AI ; Receptors, Immunologic--physiology--PH

CAS Registry No.: 0 (Adjuvants, Immunologic); 0 (Cytoskeletal Proteins); 0 (Phosphoproteins); 0 (Proteins); 0 (RBL2 protein, human) ; 0 (Receptors, Immunologic); 0 (paxillin); 50-02-2 (Dexamethasone)

Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.- (protein-serine-threonine kinase (rac)); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.37 (Protein-Serine-Threonine Kinases)

Record Date Created: 20010706
Record Date Completed: 20011004

20/9/12 (Item 12 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

13699138 PMID: 11343423

Pyk2 expression and phosphorylation in neonatal and adult cardiomyocytes.

Bayer A L; Ferguson A G; Lucchesi P A; Samarel A M

The Cardiovascular Institute, Loyola University Chicago Stritch School of Medicine, 2160 South First Avenue, Maywood, IL 60153, USA. abayer@lumc.edu

Journal of molecular and cellular cardiology (England) May 2001, 33 (5) p1017-30, ISSN 0022-2828 Journal Code: 0262322

Contract/Grant No.: F32 HL10313; HL; NHLBI; HL34328; HL; NHLBI; HL56046; HL; NHLBI; HL63711; HL; NHLBI

Publishing Model Print

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

A. L. Bayer, A. G. Ferguson, P. A. Lucchesi and A. M. Samarel. PYK2 Expression and Phosphorylation in Neonatal and Adult Cardiomyocytes. Journal of Molecular and Cellular Cardiology (2001) 33, 1017-1030. Proline-rich tyrosine kinase (PYK2) is a Ca(2+)-dependent, non-receptor protein tyrosine kinase involved in growth factor signaling. Although PYK2 is expressed in a variety of tissues, it has not yet been identified in cardiac muscle. Therefore, immunocytochemical and Western blotting techniques were used to examine PYK2 expression and phosphorylation in neonatal and adult rat ventricular cardiomyocytes (NRVM and ARVM, respectively). PYK2 concentration was much greater in neonatal, than in adult ventricular tissue and cardiomyocytes. In cultured cells, PYK2 expression was highly dependent on [Ca(2+)](i)transients and contractile activity. Non-contracting, low-density NRVM in serum-free culture expressed very low **levels** of **PYK2** , while high-density, spontaneously contracting NRVM showed a approximately 12-fold **increase** in PYK2 expression. Conversely, high-density NRVM treated with nifedipine (10 microM, 48 h) to block spontaneous [Ca(2+)](i)transients and contractile activity resulted in a 2.6-fold **decrease** in PYK2 levels. Similarly, overnight culture of quiescent ARVM markedly **reduced PYK2 levels** . Chronic treatment (48 h) of cultured NRVM with the hypertrophic agonist endothelin-1 (ET) (10-300 n M) did not significantly **increase PYK2 levels** , but strongly shifted the ratio of phosphorylated to total PYK2, indicating that PYK2 phosphorylation accompanies cardiomyocyte hypertrophy. Endothelin-1 also acutely activated PYK2 in both cultured NRVM, and in freshly isolated ARVM. These results suggest that PYK2 is involved in the generation of certain aspects of cardiomyocyte hypertrophy. Copyright 2001 Academic Press.

Tags: Female; Male; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.

Descriptors: *Myocardium--cytology--CY; *Myocardium--metabolism--ME; *Protein-Tyrosine Kinase--biosynthesis--BI; *Protein-Tyrosine Kinase --metabolism--ME; Animals; Animals, Newborn; Blotting, Western; Calcium --pharmacology--PD; Cells, Cultured; Culture Media, Serum-Free--metabolism --ME; Dose-Response Relationship, Drug; Endothelin-1--pharmacology--PD; Immunohistochemistry; Microscopy, Fluorescence; Nifedipine--pharmacology --PD; Phosphorylation; Precipitin Tests; Rats; Rats, Sprague-Dawley; Signal Transduction; Time Factors

CAS Registry No.: 0 (Culture Media, Serum-Free); 0 (Endothelin-1); 21829-25-4 (Nifedipine); 7440-70-2 (Calcium)

Enzyme No.: EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase)

Record Date Created: 20010509
Record Date Completed: 20010719

20/9/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12663843 PMID: 10583467

FAK+ and PYK2/CAKbeta, two related tyrosine kinases highly expressed in the central nervous system: similarities and differences in the expression pattern.

Menegon A; Burgaya F; Baudot P; Dunlap D D; Girault J A; Valtorta F
San Raffaele Scientific Institute, B. Ceccarelli and CNR Cellular and

Molecular Pharmacology Center, Milan, Italy.
European journal of neuroscience (FRANCE) Nov 1999, 11 (11) p3777-88
, ISSN 0953-816X Journal Code: 8918110
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
Subfile: INDEX MEDICUS

Focal adhesion kinase (FAK) and proline-rich tyrosine kinase 2/cell adhesion kinase beta (PYK2/CAKbeta) are related, non-receptor, cytoplasmic tyrosine kinases, highly expressed in the central nervous system (CNS). In addition, FAK+ is a splice isoform of FAK containing a 3-amino acid insertion in the carboxy-terminal region. In rat hippocampal slices, FAK+ and PYK2/CAKbeta are differentially regulated by neurotransmitters and depolarization. We have studied the regional and cellular distribution of these kinases in adult rat brain and during development. Whereas PYK2/CAKbeta expression **increased** with postnatal age and was maximal in the adult, FAK+ **levels** were stable. **PYK2** /CAKbeta mRNAs, detected by in situ hybridization, were expressed at low levels in the embryonic brain, and became very abundant in the adult forebrain. Immunocytochemistry of the adult brain showed a widespread neuronal distribution of FAK+ and PYK2/CAKbeta immunoreactivities (ir). PYK2/CAKbeta appeared to be particularly abundant in the hippocampus. In hippocampal neurons in culture at early stages of development, FAK+ and PYK2/CAKbeta were enriched in the perikarya and growth cones. FAK+ extended to the periphery of the growth cones tips, whereas PYK2/CAKbeta appeared to be excluded from the lamellipodia. During the establishment of polarity, a proximal-distal gradient of increasing PYK2/CAKbeta-ir could be observed in the growing axon. In most older neurons, FAK+-ir was confined to the cell bodies, whereas PYK2/CAKbeta-ir was also present in the processes. In vitro and in vivo, a subpopulation of neurons displayed neurites with intense FAK+-ir. Thus, FAK+ and PYK2/CAKbeta are differentially regulated during development yet they are both abundantly expressed in the adult brain, with distinctive but overlapping distributions.

Tags: Male; Research Support, Non-U.S. Gov't
Descriptors: *Brain--enzymology--EN; *Cell Adhesion Molecules--genetics --GE; *Gene Expression Regulation, Enzymologic; *Neurons--enzymology--EN; *Protein-Tyrosine Kinase--genetics--GE; Animals; Brain--cytology--CY; Cell Adhesion Molecules--analysis--AN; Cells, Cultured; Hippocampus--cytology --CY; Hippocampus--enzymology--EN; Immunohistochemistry; Neurons--cytology --CY; Protein-Tyrosine Kinase--analysis--AN; RNA, Messenger--genetics--GE; Rats; Rats, Sprague-Dawley
CAS Registry No.: 0 (Cell Adhesion Molecules); 0 (RNA, Messenger)
Enzyme No.: EC 2.7.1.- (focal adhesion protein-tyrosine kinase); EC 2.7.1.- (protein tyrosine kinase PYK2); EC 2.7.1.112 (Protein-Tyrosine Kinase)
Record Date Created: 19991228
Record Date Completed: 19991228

20/9/14 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014834291 BIOSIS NO.: 200400201924
Pyk2/Src are involved in the induction of group I mGluR - mediated ictal - like discharges in hippocampus .
AUTHOR: Zhao W (Reprint); Wong R

AUTHOR ADDRESS: Neural and Behavioral Sci. Program, SUNY Downstate Med. Ctr., Brooklyn, NY, USA**USA
JOURNAL: Society for Neuroscience Abstract Viewer and Itinerary Planner 2003 pAbstract No. 574.3 2003 2003
MEDIUM: e-file
CONFERENCE/MEETING: 33rd Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 08-12, 2003; 20031108
SPONSOR: Society of Neuroscience
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Stimulation of group I mGluRs by DHPG (50muM) induced interictal-like (120-810 ms) and ictal-like (1.5-8.6 sec) discharges in hippocampal slices. Induction of group I mGluR-mediated ictal-like discharges has been shown to be tyrosine kinase-, ERK1/2-and protein synthesis dependent. At present the signaling mechanisms underlying group I mGluR-mediated ERK1/2 activation are unknown. Activation of group I mGluR produces IP3 which elicits intracellular Ca2+ release. Depletion of intracellular Ca2+ stores by thapsigargin (10muM) or cyclopiazonic acid (20muM) blocked the induction of ictal-like discharges, while leaving the interictal-like discharges intact. Additionally, application of IP3R antagonist (2-APB, 50muM) also blocked the induction of ictal-like discharges. Above results suggested that Ca2+ store mobilization induced by group I mGluR stimulation is a necessary signaling step for the induction of ictal-like discharges. Pyk2/Src pathway has been suggested to play a role in mediating ERK1/2 activation by intracellular Ca2+ elevation in hippocampus. The Src family inhibitor (PP2, 10muM) was applied to examine the involvement of Pyk2/Src pathway. PP2 effectively blocked the induction of ictal-like discharges. In the presence of 0.3muM TTX, 20muM CPP and 20muM CNQX, changes of active status of Pyk2, Src and ERK1/2 were evaluated by using their phosphor-specific antibodies. Western blot analysis showed that stimulation of group I mGluRs by DHPG **increased** the phosphorylation **level** of **Pyk2** , Src and ERK1/2 in hippocampus. We conclude that the IP3-mediated intracellular Ca2+ release mechanism is necessary for the induction of the ictal-like discharges and that the tyrosine kinases Pyk2/Src pathway might be involved in mediating receptor stimulation to ERK1/2 activation and protein synthesis which underlies the induction of group I mGluR-mediated ictal-like discharges.

REGISTRY NUMBERS: 14127-61-8: calcium(II) ion; 18172-33-3Q: cyclopiazonic acid; 83136-88-3Q: cyclopiazonic acid; 67526-95-8: thapsigargin; 80449-02-1: tyrosine kinase
ENZYME COMMISSION NUMBER: EC 2.7.1.112: tyrosine kinase
DESCRIPTORS:
MAJOR CONCEPTS: Nervous System--Neural Coordination
ORGANISMS: PARTS ETC: hippocampus--nervous system
CHEMICALS & BIOCHEMICALS: 2-APB; CNQX; DHPG; ERK1/2; IP3; IP3R; PP2; Pyk2; Src; TTX; antibodies; calcium(II) ion; cyclopiazonic acid; group I mGluR; thapsigargin; tyrosine kinase
METHODS & EQUIPMENT: Western blotting--genetic techniques, immunologic techniques, laboratory techniques
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10064 Biochemistry studies - Proteins, peptides and amino acids
10069 Biochemistry studies - Minerals
10802 Enzymes - General and comparative studies: coenzymes
20504 Nervous system - Physiology and biochemistry
34502 Immunology - General and methods

DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Maturation of hematopoietic progenitor cells (HPC) to mature myeloid cells is regulated by extracellular cues including cytokines, chemokines, and the extracellular matrix present within the bone marrow. Although beta1-integrins and cytokines, such as SCF and SDF-1alpha, affect hematopoiesis, their mechanisms of action are not fully understood. Previous studies in our lab identified the alternative splicing and expression of a non-receptor tyrosine kinase gene, PYK2, in CD34+ progenitors from patients with chronic myelogenous leukemia. Phosphorylation of the PYK2 isoform normally predominant in hematopoietic cells, Pyk2H, was observed following beta1-integrin or CXCR-4 engagement in both normal and leukemic CD34+ progenitor cells. Full-length Pyk2, which is abnormally expressed in BCR/ABL-positive CD34+ progenitors, is also phosphorylated by these stimuli. In an effort to better understand the role PYK2 gene products play in myeloid cell proliferation and differentiation, PYK2, PYK2H, or the dominant negative-acting kinase-deficient C-terminal PYK2 fragment, PRNK, was introduced into cord blood CD34+ progenitors using a bicistronic green fluorescent protein (GFP)-containing, MSCV-based retrovirus. Following FACS isolation of CD34+/GFP+ cells, myeloid colony formation was assessed and the number of committed and primitive HPC, respectively, were enumerated using colony forming cell (CFC) and long term culture-initiating cell (LTC-IC) assays. The number of CFC among CD34+ progenitors overexpressing either Pyk2 or Pyk2H (Pyk2(H)) was decreased by 55% versus GFP-transduced controls, with significant reductions occurring within the colony forming unit granulocyte-macrophage (CFU-GM) population. Although the number of CFC and CFU-GM were not altered in PRNK expressing CD34+ cells, they contained significantly fewer LTC-IC, suggesting that inhibition of Pyk2(H) activation allows accelerated differentiation of primitive HPC. CD34+/GFP+ cells were also plated into a liquid myeloid differentiation culture, which allowed the influence of integrin engagement and/or SCF or SDF-1alpha to be evaluated during HPC proliferation/differentiation along the myeloid lineage. Significant reductions in CD14+ (myelocytes) cells were observed when control GFP-transduced cells were expanded in fibronectin (FN)-coated wells in the absence of SCF, whereas the presence of SCF in these cultures was able to override inhibitory signals originating from FN engagement. Consistent with data obtained in classical CFC assays, numbers of both CD14+ and Glycophorin-A+ (erythrocytes) cells were severely reduced in cells overexpressing Pyk2(H), but not PRNK. Furthermore, this Pyk2(H)-induced inhibition of HPC proliferation/differentiation was observed under all assay conditions. Finally, cell viability was consistently **higher** in GFP or PRNK expressing cell cultures than those containing Pyk2(H). Data presented here suggests that activation of **Pyk2** (H) may regulate multiple **levels** of myelopoiesis; such as inhibiting primitive progenitor cell proliferation/differentiation and promoting committed progenitor/mature cell death. Studies defining the stage(s) of myelopoiesis where Pyk2(H) has its effect(s) are ongoing.

REGISTRY NUMBERS: 153-87-7Q: integrin; 60791-49-3Q: integrin
DESCRIPTORS:
MAJOR CONCEPTS: Blood and Lymphatics--Transport and Circulation; Enzymology--Biochemistry and Molecular Biophysics; Immune System--Chemical Coordination and Homeostasis; Molecular Genetics--Biochemistry and Molecular Biophysics
BIOSYSTEMATIC NAMES: Retroviridae--DNA and RNA Reverse Transcribing

Viruses, Viruses, Microorganisms
ORGANISMS: retrovirus (Retroviridae)--gene vector
ORGANISMS: PARTS ETC: colony forming unit granulocyte-macrophage--blood and lymphatics, immune system; cord blood CD34 positive progenitor cell --blood and lymphatics, embryonic structure, immune system, differentiation, proliferation; erythrocyte--blood and lymphatics; hematopoietic progenitor cell--blood and lymphatics; myelocyte cell--blood and lymphatics; myeloid cell--blood and lymphatics, immune system , colony formation, differentiation, proliferation
COMMON TAXONOMIC TERMS: DNA and RNA Reverse Transcribing Viruses; Microorganisms; Viruses
CHEMICALS & BIOCHEMICALS: CD14; PRNK--expression; PYK2--carboxy-terminal fragment, focal adhesion kinase, regulation; PYK2H--unspliced isoform; fibronectin; glycophorin A; green fluorescent protein (GFP); integrin
GENE NAME: human PYK2 gene (Hominidae)
MISCELLANEOUS TERMS: myelopoiesis regulation; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
02506 Cytology - Animal
02508 Cytology - Human
03502 Genetics - General
03508 Genetics - Human
10064 Biochemistry studies - Proteins, peptides and amino acids
10802 Enzymes - General and comparative studies: coenzymes
15002 Blood - Blood and lymph studies
15004 Blood - Blood cell studies
25502 Development and Embryology - General and descriptive
31500 Genetics of bacteria and viruses
33506 Virology - Animal host viruses
34502 Immunology - General and methods
BIOSYSTEMATIC CODES:
03305 Retroviridae

20/9/20 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012937661 BIOSIS NO.: 200100109500
Expression of Pyk2 in the mesolimbic dopamine system and regulation by chronic morphine
AUTHOR: Liu S R (Reprint); Schultz H; Numan S; Wolf D H; Russell D S
AUTHOR ADDRESS: Yale School of Medicine, CMHC, New Haven, CT, USA**USA
JOURNAL: Society for Neuroscience Abstracts 26 (1-2): pAbstract No.-699.16 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000; 20001104
SPONSOR: Society for Neuroscience
ISSN: 0190-5295
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Chronic exposure to opiates produces several persistent behavioral changes thought to be consistent with addictive behaviors. These changes correlate with a number of biochemical alterations in

protein expression and activity within neurons in the mesolimbic dopamine system. Many studies have implicated this dopaminergic system with a role in at least some of these behaviors. For instance, we have found that chronic morphine exposure increases PLC-gamma in the VTA, which would be expected to increase intracellular calcium release and PKC activation. Others have found GluR1 expression increased in VTA, which may increase calcium flux. Prior studies have also demonstrated the importance of **increased** ERK activity in the VTA in mediating morphine-induced changes. We now identify a potential link between these observations. We report that **Pyk2 levels** are up-regulated by morphine in the VTA and nucleus accumbens, and that morphine **increases** the tyrosine phosphory-lation state of Pyk2, which is known to correlate with increased activity. Pyk2 has been shown to mediate ERK activation by intracellular calcium and PKC activation. We further characterize the expression and regulation of Pyk2 in the mesolimbic dopamine system.

REGISTRY NUMBERS: 7440-70-2: calcium; 57-27-2: morphine
DESCRIPTORS:
MAJOR CONCEPTS: Behavior; Endocrine System--Chemical Coordination and Homeostasis; Nervous System--Neural Coordination; Pharmacology
ORGANISMS: PARTS ETC: mesolimbic dopamine system--nervous system; nucleus accumbens--nervous system
DISEASES: addictive behavior--behavioral and mental disorders
MESH TERMS: Behavior, Addictive (MeSH)
CHEMICALS & BIOCHEMICALS: GluR1--expression; PKC (protein kinase C)--activation; Pyk2--expression; calcium--flux; morphine--chronic, pharmacodynamics
MISCELLANEOUS TERMS: chronic opiate exposure; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
10069 Biochemistry studies - Minerals
00520 General biology - Symposia, transactions and proceedings
07002 Behavioral biology - General and comparative behavior
07004 Behavioral biology - Human behavior
10060 Biochemistry studies - General
10802 Enzymes - General and comparative studies: coenzymes
12512 Pathology - Therapy
17002 Endocrine - General
17020 Endocrine - Neuroendocrinology
20504 Nervous system - Physiology and biochemistry
21004 Psychiatry - Addiction: alcohol, drugs, smoking
22002 Pharmacology - General

20/9/22 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012903473 BIOSIS NO.: 200100075312
Tyrosine kinase CAKbeta/Pyk2 is an intermediary in induction of long-term potentiation in CA1 hippocampus
AUTHOR: Ali D W (Reprint); Huang Y Q; Lu Y M; Aoto H; Sasaki T; Salter M W
AUTHOR ADDRESS: Univ. Toronto, Toronto, ON, Canada**Canada
JOURNAL: Society for Neuroscience Abstracts 26 (1-2): pAbstract No.-38.6 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000; 20001104
SPONSOR: Society for Neuroscience

ISSN: 0190-5295
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The biochemical cascade producing long-term potentiation (LTP) requires activation of the tyrosine kinase Src which upregulates the function of NMDA receptors (Lu et al. Science 279, 1363, 1998). A central unresolved question is how Src becomes activated. We have found that a member of the focal adhesion kinase family, CAKbeta/Pyk2, upregulates NMDA receptor function by activating Src. Here, we tested the hypothesis that CAKbeta/Pyk2 mediates LTP induction at Schaffer collateral-CA1 synapses in hippocampal slices using whole-cell and field recordings. Intracellularly administering CAKbeta/Pyk2 into CA1 neurons increased EPSP slope to 317+-54%(mean+-SEM) of the baseline level and occluded induction of LTP by tetanic stimulation (n=6 cells). The increase in EPSP slope produced by CAKbeta/Pyk2 was prevented when the Src inhibitor peptide, Src(40-58), was included in the intracellular solution (n=5) or by bath applying the NMDA channel blocker MK-801 (n=3). During intracellular application of the dominant negative mutant, K457A CAKbeta/Pyk2, EPSP slope was 105 +-6% of baseline, 30 min after tetanic stimulation (n=8), whereas in control cells EPSP slope was 172+-15% baseline 30 min after tetanus (n=12). With K457A CAKbeta/Pyk2 tetanus caused a long-lasting increase in the slope of field EPSPs that was not different from the slope of field EPSPs evoked in control recordings (P>0.05). Thus, K457A CAKbeta/Pyk2 prevented the induction of LTP in the cells in which it was administered intracellularly, but not in neighbouring neurons. The **level** of tyrosine phosphorylation of CAKbeta/**Pyk2** and the association of CAKbeta/Pyk2 with Src was **increased** by the tetanic stimulation that produced LTP. Together these results indicate that activating CAKbeta/Pyk2 is necessary and sufficient for inducing LTP, and may depend upon downstream activation of Src to upregulate NMDA receptors.

DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Nervous System--Neural Coordination
BIOSYSTEMATIC NAMES: Animalia--Animalia
ORGANISMS: animal (Animalia)
ORGANISMS: PARTS ETC: CA1 hippocampus--nervous system
COMMON TAXONOMIC TERMS: Animals
CHEMICALS & BIOCHEMICALS: N-methyl-D-aspartate receptor; Src--downstream activation; tyrosine kinase CAK-beta/Pyk2--intermediary
MISCELLANEOUS TERMS: biochemical cascade; long-term potentiation--induction; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
10064 Biochemistry studies - Proteins, peptides and amino acids
00520 General biology - Symposia, transactions and proceedings
10060 Biochemistry studies - General
20504 Nervous system - Physiology and biochemistry
BIOSYSTEMATIC CODES:
33000 Animalia

20/9/24 (Item 1 from file: 71)

01279539 1999260891